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JANUARY 1956 VOLUME 72 NUMBER 1

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Gerald H. Pratt

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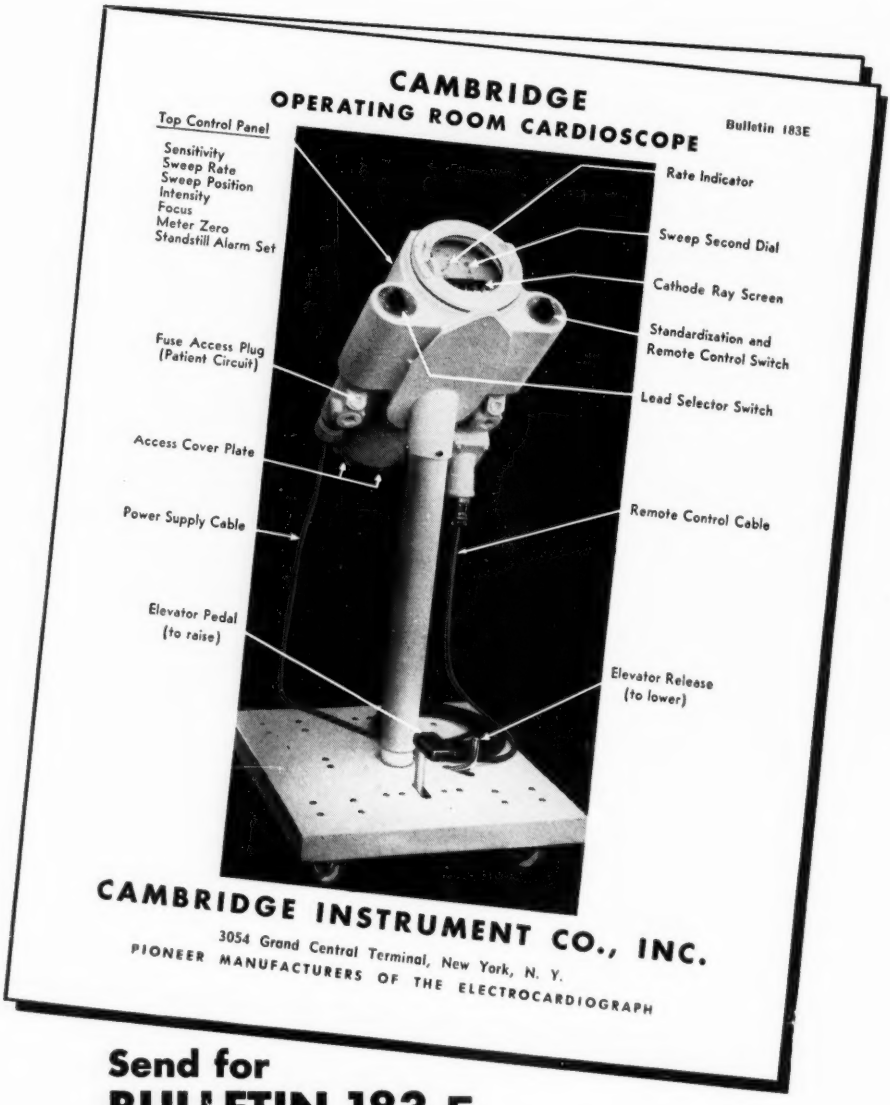

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A.M.A. Archives OF SURGERY

Dr. Rudolph Matas

ALTON OCHSNER, M.D., New Orleans

Surgery of the vascular system has progressed tremendously in the past 70 years, and the one man who has been most responsible for this advance is Rudolph Matas, who today at 95 years of age is as keenly interested in innovations pertaining to the vascular system as he was when he performed his first endoaneurysmorrhaphy, on May 6, 1888. The story of Dr. Matas' accomplishments sounds like a fairy tale, because it seems impossible that any one man could have done so much in a lifetime and could have been responsible for so many "firsts."

Dr. Matas was born on Sept. 1, 1860, at the Bonnet-Carre, St. John Parish, a short distance from New Orleans. His mother and father were Spanish. His father, Dr. N. Hereu Matas, was a prominent oculist in Brownsville, Texas. When Dr. Matas was two years of age, his parents returned to Spain. They lived for the following eight years in Barcelona and in Paris, and Dr. Matas became proficient in both the Spanish and French languages and was able to speak them and even the Spanish dialect "Catelon" without any accent. In 1868, the Matas family returned to Brownsville, Texas. While still a youngster, young Rudolph attended Soule College in New Orleans for three years and then returned to Matamoros, Mexico, where he finished his academic education at the San Juan Institute in 1876. In 1877 he matriculated in the Medical Department of the University of Louisiana, which is now Tulane University of Louisiana. At the completion of his first session, he competed for the position of resident student at the Charity Hospital and was successful in winning the appointment, even though there was a great deal of political pressure to appoint some of the political favorites. In 1878 he participated in the fight against the yellow fever epidemic and became familiar with the disease. In 1879, while still a student, he was appointed as interpreter of the

Fig. 1.—Dr. Matas, in 1879, as interpreter of the Yellow Fever Commission of the National Board of Health. Dr. Matas is in the background.

Submitted for publication July 28, 1955.

From the Department of Surgery, School of Medicine, Tulane University and the Ochsner Clinic.

Presented at the Third Scientific Meeting of the North American Chapter of the International Society of Angiology, Atlantic City, N. J., June 4, 1955.

Fig. 2.—Dr. Matas in Havana, Cuba, on Sept. 12, 1879, as clerk for the Yellow Fever Commission. Dr. Matas is standing, the second from the left.

Yellow Fever Commission of the National Board of Health and went with the Committee to Cuba to study the disease (Figs. 1 and 2). In 1880, while an intern at the Charity Hospital, he assisted at the first laparotomy performed under Listerian ritual, including the use of carbolic acid spray. In March, 1880, he received his Doctor of Medicine degree from Tulane University. In 1882, as a young physician, he was called to Mier, Mexico, to treat the epidemic of yellow fever in that city. In 1886 he was appointed Demonstrator of Anatomy at Tulane University, which position he held until he was appointed Professor and Chairman of the Department of Surgery, in 1894 (Fig. 3), and held this position until his retirement, in 1927.[1]

Dr. Matas' first endoaneurysmorrhaphy was performed on May 6, 1888, more than 67 years ago. This case is of sufficient historical significance to describe it somewhat in detail. The patient was a young Negro, aged 26, who had been admitted to Dr. Matas' ward at Charity Hospital because of a large traumatic aneurysm of the brachial artery in its middle third resulting from being shot with fine bird shot approximately two months previously.[2] When the patient was first admitted to the hospital, an attempt was made to control the aneurysm by conservative measures. A Massachusetts General Hospital compressor was applied to the brachial artery above the aneurysm. The patient was able to tolerate the compressor for approximately 40 minutes, when the pain became intolerable. This method of therapy was used for three weeks, applying the compressor repeatedly so that the artery was compressed most of the time. During this time, however, the aneurysm became larger. It was, therefore, decided to operate upon the patient. The brachial artery was ligated in its upper third, just below the superior profunda and immediately above the aneurysm. After this, there was immediate cessation of pulsation in the aneurysm. The condition improved, but nine days later it was noticed that there was slight pulsation of the tumor, which became progressivly more marked daily until it became as pronounced, and the tumor became as painful as it had been when the patient was first seen. Two weeks after the proximal ligation, on May 6, it was decided to ligate the vessel immediately below the aneurysm. This was done in a bloodless field after the application of an Esmarch bandage. After the ligation immediately below the aneurysm, following the removal of the Esmarch bandage, there

Fig. 3.—Dr. Rudolph Matas, Professor of Surgery, Medical Department of Tulane University of Louisiana, 1894.

was no decrease in pulsation of the aneurysm. The Esmarch bandage was then reapplied, and it was decided that the aneurysm should be excised if possible, but after the aneurysm was exposed this was found to be impossible, owing to the intimate connection of the sac with the important or deeper structures of the arm, especially the biceps and the brachialis anticus. The dissection and isolation of the sac were, therefore, stopped and a large incision made throughout its whole length; at the same time an elliptical piece of sac, representing its exposed portion, was excised, and the clot which was partially laminated, but mostly passive, in its central parts, was turned out in larger quantities, the whole cavity being constantly and thoroughly irrigated with a 1:2000 acid sublimate solution ("Laplace's"). By this means, three orifices were readily detected at the bottom of the sac, two of these being large enough to admit readily a number 8 gum catheter; the middle orifice only offering some resistance to catheterization.

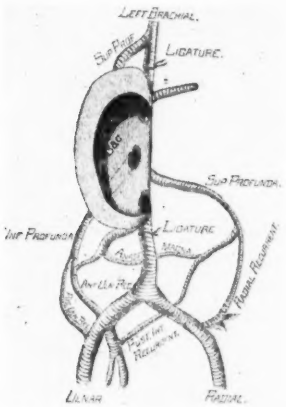


Fig. 4.—Dr. Matas' original drawing of aneurysm in which the first endoaneurysmorrhaphy was performed. (From Matas,[2] *Medical News*, Philadelphia.)

A gum catheter was first passed into the orifice nearest the axilla, and it readily passed upward inside the artery until it stopped at a point where the first ligature had been applied sixteen days previously, proving clearly that that was the proximal axillary end of the aneurysm. A catgut ligature was once more applied while the catheter was in situ, the catheter, which served as a perfect guide, being withdrawn as the ligature was tightened. Introduction of the catheter into the lower orifice led at once to the bend of the elbow, where it was arrested at a point where the ligature had just been applied. It remained now to close the third or middle orifice, which was small and apparently had no connection with the two preceding; this orifice I presumed to be the orifice of a much dilated inferior profunda. This orifice was completely sealed by passing four fine interrupted silk sutures (for want of fine catgut) through its lips. The Esmarch constrictor was then relaxed, and I was considerably surprised to notice a decided flow of blood from the other two orifices notwithstanding the fact that the vessels with which they communicated had been apparently controlled by previous ligature at the proximal and distal extremities of the sac; this showed plainly that there must be some important collaterals which communicated with the vessels between the points of ligature and internal or aneurysmal orifices. In view of this, I immediately stitched the lips of the orifices with fine, sublimated silk, by which means the openings were sealed completely and not a drop of blood entered the sac henceforth [Fig. 4]. Following this, the patient got along very well.

Thus, the operation of endoaneurysmorrhaphy, for which Dr. Matas is so widely known, was devised. Because of Dr. Matas' ingenuity and imagination he was able to cope with the situation which presented itself in operating upon this patient in 1888. In 1898, ten years later, the patient was well. In commenting on this case in 1898, Dr. Matas stated:

At the time this operation was performed, I had not precedence to guide me, the only work that had been done, was that of Glueck, published in Langenbeck's Archives, in which he detailed 19 experiments in the suture of arteries which had failed to a great extent in spite of ingenious methods that he had devised. The exigencies of the case, however, made it necessary that hemostasis should be obtained, and the occlusion by suture appeared to be so easy and plain that it seemed to me that any surgeon similarly situated would have instinctively adopted this simple way of getting out of the difficulty.

A long interval elapsed between this and the next case which occurred in my practice and which I operated in 1900 by more advanced technique. Several opportunities had presented themselves for the application of the suture method for aneurysms in my practice in the interval between 1888 and 1900, but I had not mustered enough courage to battle with tradition which had imbued me as it did most every operator with the fear of the dangers of atheroma and secondary hemorrhage in suturing injured arteries, but disastrous results which followed in the case of a femoral aneurysm treated by

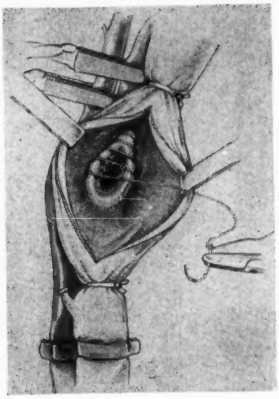
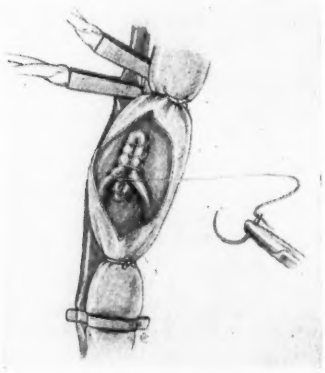


Fig. 5.—One of Dr. Matas' original drawings of technique of closure of arteriovenous fistula. "Interior of the sac exposed by opening the anterior venous wall. The method of obtaining hemostatic control is shown. The single orifice of communication with thickened edges is closed by continued suture." (From Matas,[12] *Transactions of the Southern Surgical Association,* Philadelphia.)

the Hunterian ligation in which gangrene had occurred immediately after the simple ligation, compelling me to perform an amputation of the thigh to save the man's life; and also the vivid recollection of the difficulties which I had encountered in the extirpation of another femoral aneurysm in Scarpa's triangle, in which gangrene of the toes occurred as a sequel of ligation of the artery, led me again to revert to the advantages of a modified Antyllian operation, as I performed it in 1888 in my first case.[5]

The opportunity presented itself in 1900 when a white farmer, aged 32, was brought to me for the

Fig. 6 (continuation of Fig. 5).—Obliteration of the sac by infolding and suturing the venous walls in superimposed layer after closure of the orifice. (From Matas,[12] *Transactions of the Southern Surgical Association,* Philadelphia.)



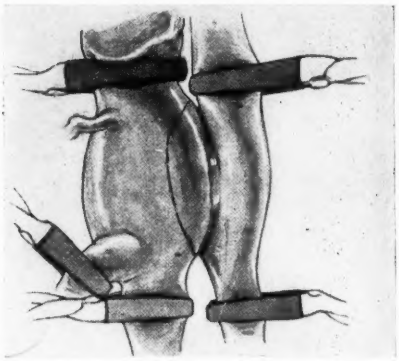


Fig. 7.—An original Matas drawing of technique of treating arteriovenous fistula. "Detail of anastomosis to show line of incision on the vein in order to expose the interior of the sac." (From Matas,[12] *Transactions of the Southern Surgical Association,* Philadelphia.)

treatment of a traumatic aneurysm of the right brachial involving the upper third of the vessel.

An endoaneurysmorrhaphy was done with complete cure.

In a presentation before the American Surgical Association in 1902,* Dr. Matas commented on the many advantages of the operation of endoaneurysmorrhaphy and reported four cases (Figs. 5 to 9).

Dr. Matas continued to have considerable experience in the treatment of vascular

* Reference 7 and 8.

Fig. 8 (continuation of Fig. 7).—"Interior of the sac, showing closure of the orifice of communication by continued silk suture." (From Matas,[12] *Transactions of the Southern Surgical Association,* Philadelphia.)

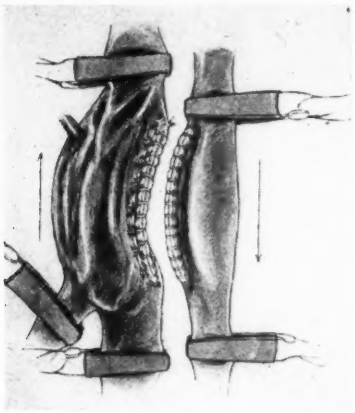
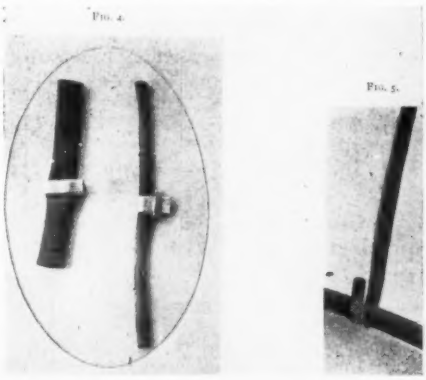


Fig. 9 (continuation of Figs. 7 and 8).—"The anastomosis closed; artery and vein detached, isolated and separately closed by lateral arterio- and phleborrhaphy. The arterial orifice has been closed separately by intrasaccular suture on the venous side and the first line of intrasaccular sutures is reinforced at the expense of the vein." (From Matas,[12] *Transactions of the Southern Surgical Association,* Philadelphia.)

lesions, primarily because of the tremendous number of such cases admitted to the Charity Hospital in New Orleans and also because of his intense interest in the subject. He and his staff did a great deal of laboratory investigative work on temporary occlusion of vessels and developed an aluminum band which could be applied to an artery for varying periods of time without injury to the vessel, permitting release of the obstruction if such became necessary. The use of the aluminum band was particularly important in determining whether one could occlude the carotid. Dr. Matas, in his presidential address before the American Surgical Association, in June, 1910,[4] described experiments done by him and Dr. Allen demonstrating that an aluminum band can be applied to major arteries for varying periods of time without injury to the vessel (Fig. 10). In a subsequent report by Drs. Matas and Allen before the American Medical Association in 1910,[3] the results of their extensive experimental investigation were presented. The investigations had been conducted over a three-year period, from 1908 to 1910, and included gross and microscopic examinations of major arteries which had been occluded with aluminum bands for varying periods of time (one to six days). The investigation demonstrated that it was possible to compress a vessel to the point of obliteration of the pulse and maintain this pressure for three to four days without the development of obliterative endarteritis and that all vessels clamped in this manner withstood compression 72 hours without recognizable gross visible changes but that some of them developed changes in 96 hours.

In an extensive report before the Southern Surgical and Gynecological Association, in November, 1900,[5] Dr. Matas described the treatment of aortic abdominal aneurysm by preliminary laparotomy, with peritoneal exclusion of the sac followed later by wiring of the aneurysm and electrolysis. The first patient he reported was a man aged 23 who had a large abdominal aortic aneurysm. Dr. Matas first saw him on May 28, 1900. He was operated upon on June 5, at which time the pancreas and splenic vessels were mobilized and displaced upward, leaving a space overlying the aneurysm representing the free peritoneal surface of the aneurysm. The parietal peritoneum was then sutured to the periphery of this area, and this portion of the incision was left open. The patient was

Fig. 10.—Original Matas photographs on use of aluminum band to occlude blood vessels. "Types of removable aluminum bands used to occlude the arteries. The aluminum band used as an aneurysm needle, it is readily adjusted in this shape to the contour of the artery." (From Matas,[4] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)



treated conservatively but with no improvement. On July 5, 1900, under topical cocaine analgesia, the aneurysm was needled according to the MacEwen plan.

A long sterile steel hatpin was used for this purpose, and its point was made to rub gently over the posterior and lateral walls of the sac. Two aseptic needles were introduced and left in situ for one and a half hours, after which they were removed and the punctures closed with collodion and cotton. No local noticeable change followed this procedure, and in view of the patient's progressive decline, we decided to give him the advantage of wiring combined with electrolysis (Moore-Corradi-Stewart method). After considerable experimentation with various kinds of wire and artificial aneurysms (bladders, rubber balloons, and bottles), it was finally decided to use drawn silver wire. This wire was especially made by a manufacturing jeweler and formed a perfect coil after passing through a four inch straight needle. This wire, when drawn, corresponded in size to the No. 00 Hartman combination spool wire such as used for banjo strings and is about 28 gauge and about .0085 inch in diameter. A four inch pointed cannula (caliber of a No. 2 Dieulafoy aspirating needle) was insulated (by professional electrician) by coating with shellac and tried with the wire, which fed through it without trouble.

On July 9, under topical cocaine analgesia, 10 feet of the wire was introduced into the aneurysm. With a galvanic battery ("dry chloride of silver cells"), electrolysis was performed for 4 hours and 20 minutes—with a milliamperage varying from 85 to 210. The patient was temporarily benefited but within 3 days became worse and died 19 days after the wiring and electrolysis, of rupture of the aneurysm.

Dr. Matas reported another case in which wiring of the aneurysm with steel wire was accomplished. The patient survived the wiring by 45 days; the wire was found at autopsy to extend throughout the whole length of the aorta and could actually be seen in the ventricle of the heart. He reviewed seven other reported cases.[6]

In 1925, and again in 1940, before the American Surgical Association,[16] Dr. Matas reported a case of ligation of the abdominal aorta in a Negro woman aged 28, for an aneurysm involving both common iliac arteries including bifurcation of the aorta (Figs. 11-16). This is the first record of aortic ligation. In April, 1923, the aorta was ligated immediately above the sac with two ½ in. cotton ligatures in juxtaposition. This was followed by immediate cessation of all pulsation and circulation of the sac and disappearance of pulses of the lower extremity. The mass became progressively less, and the murmur and pulsation in the mass disappeared on the right side of the sac, whereas the left side still pulsated vigorously but was firmer and reduced in size. The aneurysm was apparently cured immediately after operation, but for about nine days the patient was in a precarious condition with threatened cardiorespiratory failure. She had passive congestion, patchy lobar pneumonia, and pulmonary edema. However, she was relieved of her symptoms when there was return of minimal pulsations in the aneurysmal sac and in the femoral arteries in the groins. Apparently the ligatures yielded sufficiently to allow a small reduced stream to flow through the segmented ligated segment, which converted the total artesia into a partial stenotic occlusion. One year after operation, the patient was apparently cured. However, shortly after this she developed evidence of cervical tuberculous lymphadenitis. On Sept. 10, 1924, she died suddenly of pulmonary hemorrhage from a tuberculous cavity of the lung.[17] It was the consensus of those who examined the autopsy specimen that the relaxation of the ligature was not caused by slipping of the knots but by permeation and erosion of the cotton fibers of the ligature material. The intima of the narrowed area was intact, permitting the persistence of a small opening in the vessel.

Many other subsequent reports were made by Dr. Matas.† In a very extensive report made before the American Surgical Association in St. Louis, on May 2, 1940, Dr. Matas described his experiences in vascular surgery. He reported a total of 620 operations for aneurysm, of which 101 had been treated by suture methods. Of these 101, there were 68 obliterative endoaneurysmorrhaphies for

† References 9 to 15.

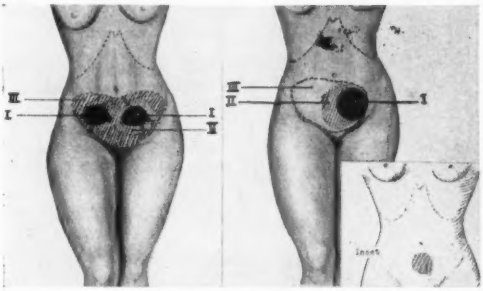
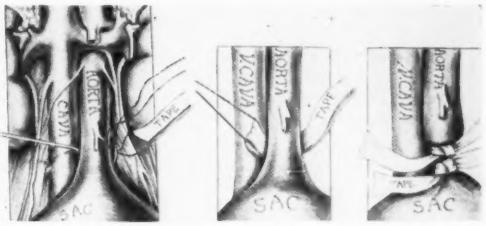


Fig. 11.—Original Matas drawing of abdominal aneurysm in which the first successful aortic ligation was performed. "Diagrammatic outline of tumor area to show the two centers or vortices of the greatest circulatory activity before the operation. I. Bilateral centers of loudest murmurs and most vigorous pulsation. II. Middle zone of moderate pulsation and bruit. III. Outer zone of least intensity. Diagrammatic outline of contracting area of tumor as felt, April 8, 1924, one year after the ligation of the aorta. I Contracting center of pulsation and feeble bruit. II. Zone of less active pulsation and inaudible bruit. III. Zone of totally absent pulsation and bruit in gradually shrinking sac. Inset—Area of palpable tumor felt, June 14, 1924, two months after the preceding observation (14 months after ligation), as a small, fixed, hard, pulseless and silent mass in the infraumbilical region, about size of a small mandarin orange. It was now evident that the clot in the sac had consolidated and the aneurysm had ceased to be active." (From Matas,[18] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)

Fig. 12 (continuation of Fig. 11).—"Ligation of the aorta immediately above the sac. One-half inch cotton tape led around artery by catgut traction loop and aneurysm needle. Continuation of this action. Tape cut in two and applied as double ligature to the artery. Upper tied first; shows first hitch in knot." (From Matas,[18] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)



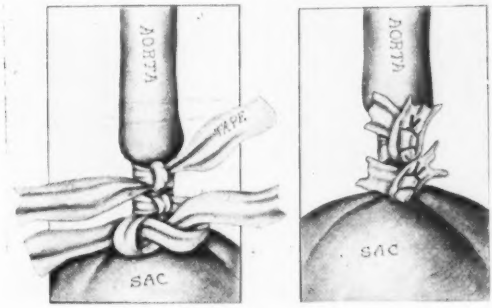


Fig. 13 (continuation of Figs. 11 and 12).—"Both ligatures in place. Second knot being tied on lower ligature; second knot already tied in upper ligature. Both knots tied. Knots secured by through-and-through silk sutures to prevent slipping. The free edges of the tapes were cut short to reduce their bulk." (From Matas,[18] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)

aneurysm; 25, restorative endoaneurysmorrhaphies for aneurysm; 5, reconstructive endoaneurysmorrhaphies for aneurysm; one, circular angiorrhaphy, popliteal, following excision for a myxosarcoma, and 2, sutures of axillary wounds following radical extirpation for a malignant neoplasm. There were 519 with occlusion of arteries by band, ligature, or other methods for all causes. There were 89 in which bands were applied, 77 for aneurysm and 12 for conditions other than aneurysm. There were 402 ligations, 47 for single ligations for aneurysm, 15 quadruple ligations for arteriovenous aneurysm, and 340 for conditions other than aneurysm. There were eight excisions, three for aneurysm and five for conditions other than aneurysm, six wirings for aneurysm, three exploratory laparotomies for aneurysm with no wiring, five clampings for aneurysm and wounds, one aneurysmotomy and plugging of orifice of wounded artery in vertebral canal for aneurysm, one intrasaccular ligation for aneurysm, two mechanical compressions, popliteal, and two amputations for popliteal injuries, gangrenous on ad-

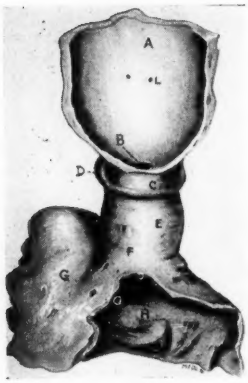
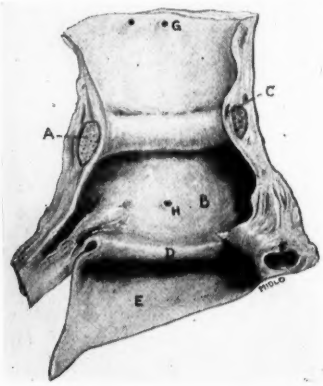


Fig. 14 (continuation of Figs. 11, 12, and 13).—"Semidiagrammatic sketch of lower abdominal aorta at the ligation; anterior view. A., aorta cut open as far down as ligature; B., newly formed lumen; C., position of cotton tape ligatures; D., bulge due to knots; E., pouchlike portion of aorta between ligatures and internal tissue shelf at F.; G., surface, and H., interior of aneurysmal sac which has largely been cut away; L., orifice of fourth lumbar artery." (From Matas,[18] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)

mission. In the sum total there were 519 total exclusions, with 25 deaths, a mortality rate of 4.81%. There were 101 operations in which suture was used, with 5 deaths, a mortality rate of 4.9%.

Fig. 15 (continuation of Figs. 11, 12, 13, and 14).—"Internal view of lower abdominal aorta at the ligation. The anterior wall of the aorta and sac have been cut longitudinally to expose the lumen surface. A., cotton tape ligatures; B., pouchlike portion of aorta between ligature and internal tissue shelf; D., C., area of calcification; E., wall of aneurysmal sac; F., left common iliac artery; G., orifice of fourth lumbar artery; H., orifice of middle sacral artery." (From Matas,[18] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)



Dr. Matas has emphasized the systemic effects of arteriovenous aneurysm and has called attention to the desirability of delaying repair in these in order to favor the development of collaterals. He popularized Branham's sign, which was first described by Dr. Harris Branham, of Georgia, in 1890. He believes that this sign is not only of diagnostic but of prognostic value in arteriovenous aneurysm.‡

Another contribution which Dr. Matas made to vascular surgery was the elaboration of the hyperemic test to determine the adequacy of collateral circulation following obliteration of a vessel.§ This consists of compressing the parent vessel proximal to

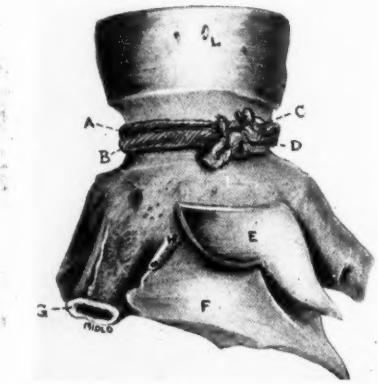


Fig. 16 (continuation of Figs. 11, 12, 13, 14, and 15).—"Posterior view of lower abdominal aorta at the ligation. The anterior wall of the aorta and sac have been cut longitudinally. The entire outer aspect of the vessel wall is shown. The tissues covering the outer surface of the ligatures have been dissected away, exposing the two pieces of cotton tape A. and B., and their knots, C. and D.; E., a small portion of the inferior vena cava; F., the upper portion of the aneurysmal sac; G., the left common iliac artery; H., middle sacral artery; L., orifice of fourth lumbar artery." (From Matas,[18] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)

an aneurysm sufficiently to obliterate it and then emptying the extremity of blood by applying an Esmarch bandage. While the compression of the parent vessel is still maintained sufficiently to prevent any pulsation of the aneurysm, the Esmarch is quickly

‡ References 21 and 22.

§ References 19 and 20.

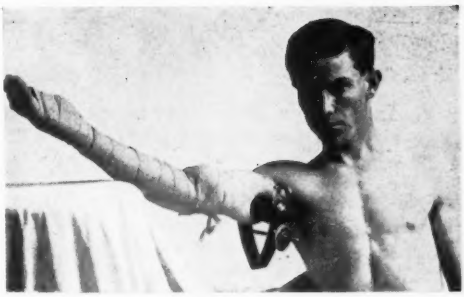


Fig. 17.—Original Matas photograph illustrating technique of Matas test for determining adequacy of collateral development. "The compressor applied to the upper brachial artery. The elastic bandage should be applied more completely over the padded fingers than is shown in the photograph. The band should not extend beyond the upper pole of the aneurysm. The upper pole should be exposed to permit the finger of the observer to determine the absence or presence of pulsation." (From Matas,[4] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)

removed. The returning wave of hyperemia is carefully observed, and in this way one can determine the adequacy of the collateral circulation by the extent and rapidity of the hyperemia (Figs. 17 and 18).

Dr. Matas' interest in vascular disease is not limited to the arterial system, but he has exhibited considerable interest and done a great deal of work on venous thrombosis, postoperative embolism, and postphlebitic sequelae.

He has done more than anyone else in the United States to emphasize the role played by edema in the production of recurrent erysipeloid infections of the extremity. In 1911, in a discussion before the Southern Surgical Association,[23] he described the mechanism of the development of elephantiasis and suggested treating recurrent erysipeloid infections (originally described by the German dermatologist, Unna) by injections of antistreptococcic serum. In a very extensive report in 1913,[24] this condition is described in a most complete manner:

> By elephantiasis we mean a progressive histopathologic state or condition which is characterized by a chronic inflammatory fibromatosis or hypertrophy of the hypodermal and dermal connective tissue which is preceded by and associated with lymphatic and venous stasis and may be caused by any obstruction or mechanical interference with the return flow of the lymphatic and venous currents in the affected part. In order to bring about the hypertrophy of the connective tissue which is a distinctive feature of the true elephantiasic state the mechanical impediment to the lymphatic and venous drainage to the part is not sufficient because a simple mechanical obstacle while causing a regional or localized dropsy or lymphedema, will not bring about the characteristic fibromatosis and other histologic changes which are peculiar to elephantiasis. As Unna, Darier, and many others have well shown, a simple mechanical edema is incapable of exciting a proliferation of the collagenous connective tissue. We know by clinical observation that edema may exist many years in the extremities and other parts without causing any fibromatosis or hyperplasia of the connective tissues of the parts. Something more than lymph stasis is required and that something is infection with pathogenic organisms, and especially those of the streptococcal type which find a favorable soil for development in the stagnant lymph stream. The histopathological elements which are essential to complete the picture of elephantiasis are: (1) mechanical obstruction or blockade of the veins and lymphatics of the region, usually an obliterative thrombophlebitis or lymphangitis or adenitis, (2) hyperplasia of the collagenous connective tissue of the hypoderm, (3) gradual disappear-

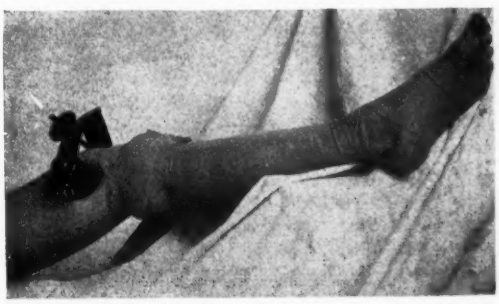


Fig. 18 (continuation of Fig. 17).—"The compressor applied to the femoral at Hunter's canal. The same defective application of the elastic bandage occurs in this illustration as in the preceding photograph; the toes should have been completely covered by the elastic bandage." (From Matas,[4] *Annals of Surgery,* Philadelphia, J. B. Lippincott Company.)

ance of elastic fibers of the skin, (4) the existence of a coagulable dropsy or hard lymphedema, and (5) a chronic reticular lymphangitis caused by secondary and repeated invasion of pathogenic microorganisms of the streptococcal type.

Dr. Matas also performed the first Kondoleon operation that was done on the Western Hemisphere. The original communication by Kondoleon was in the *Zentralblatt für Chirurgie* on July 27, 1912. Dr. Matas' first Kondoleon operation was performed on Oct. 20, 1912.

In a report before the International Society of Surgery in Warsaw in July, 1929,[25] Dr. Matas emphasized the importance of the increased incidence of thromboembolism. A very complete discussion of the subject of thromboembolism was given in the Donald Balfour Lecture, at the University of Toronto, April 5, 1932,[26] in which he emphasized that the tremendous increase in the incidence of thromboembolism was associated with modern surgery and that before Listerism it was a rare disease. He emphasized the importance of increased coagulability of the blood resulting from tissue injury as a factor in causing venous thrombosis.

One of the best presentations on primary thrombosis of the axillary vein was published by Dr. Matas in 1934,[27] in which he emphasized the role which effort or strain plays in its development.

Among the other "firsts" which Dr. Matas performed was the use of intravenous saline infusion in surgical patients. In a report made in 1891 [28] he states, "It is, I believe, historically correct to state that no attempt prior to July, 1888, had been made to infuse intravenously saline solution for the relief of acute anemia." He quotes a case of a man 26 years of age who had had an amputation of his leg for a cavernous sarcoma of the thigh.

> The hemorrhage was comparatively slight (not over 3 ounces), the vessels in the posterior flap being readily controlled with the able assistance of Dr. Laplace. Notwithstanding the really small loss of blood the patient was in a condition of profound shock when he was placed in bed, the pulse being very small, shallow, and rapid. Brandy and ammonium carbonate were administered and heat applied to the body and extremities. The patient recovered consciousness in the course of an hour and spoke intelligently. He vomited or rather strained with nausea considerably. Six hours after operation I visited the patient and found him perfectly rational and talkative though profoundly prostrated, the pulse being intermittent and extremely shallow and rapid. Notwithstanding the persistent application of heat the patient was growing colder and a clammy sweat bathed the surface. I now decided to try the effects of an intravenous saline solution. Two pints of a common salt solution made by boiling one gram of common salt in a pint of distilled water were slowly injected into the median basilic vein. The fluid was infused warm (about 100°F.). A few seconds after the injection had commenced the patient gave utterance to expressions of increasing comfort and grateful well-being. He had complained of a "fire" or "heat" which was consuming his vitals and "great burning thirst." Now, as the water flowed into the vein, he felt as if a delightful cool wave were gently spreading over his body and was giving him new strength and life and wonderfully appeasing his thirst. The pulse in the meantime improved immensely, it became fuller, more resistant to the finger, then slower, and finally quite strong and regular, the pulsation having been reduced from 150 to 100 and less when the injection was stopped.
>
> The patient was apparently better the next morning; however, that evening,
>
> the patient is evidently relapsing into the same condition as before saline injection, the beneficial effects of which are now no more perceptible, the pulse is practically imperceptible at wrist and a cold clammy sweat bathes the surface, he is manifestly sinking. I again inject nearly two pints of the same saline solution into the left median basilic. This time the pulse responds more slowly to the influence of injection and requires more fluid than the first time to fill it up. After the second pint the pulse, however, rallies and becomes hard and the patient revives. The beneficial effects of this injection are more transitory than the first, the newly improved pulse is maintained only a quarter of an hour, the pulse becoming rapidly faster and weaker, so that in the course of three or four hours it becomes imperceptible, consciousness lost, and the patient expired on the morning of the sixteenth.

In remarking on this case, Dr. Matas believed that the prostration was due to shock and not hemorrhage because he felt that the hemorrhage was not sufficient to cause death. He then cites 18 other patients who were treated with saline solution and summarizes the 18 as follows:

There were 6 due to hemorrhage of which 5 recovered, there were 2 due to hemorrhage and shock both of whom recovered, there were 3 due to shock and hemorrhage all of whom died, there were 3 due to shock all of whom died; there was one due to acute exhaustion who also died, there were 3 due to exhaustion and hemorrhage all of whom died, there was one due to exhaustion and shock who also died.

His first description is an excellent one of the temporary effect of increasing the blood volume with a noncolloidal solution in a person who obviously had a contracted blood volume even though relatively little blood had been lost. It is understandable that, in 1891, he should not appreciate the significance of a contracted blood volume.

Dr. Matas was also one of the first to advocate gastric drainage, and, in a report in 1924,[6] he emphasizes the value of the use of the indwelling Jutte tube introduced through the nose. He states, "By draining the stomach, the gastric tube acts in reality as an artificial anus which empties the upper intestine of its toxic contents and diminishes the abdominal distention caused by pent up gases, thereby adding enormously to the comfort of the patient." [29]

Because of Dr. Matas' interest in vascular surgery it is only natural that he would be interested in procedures which would facilitate the performance of operations within the thorax, and he did considerable work on overcoming the disastrous effects of acute surgical pneumothorax. At a meeting of the Southern Surgical and Gynecological Association held in November, 1899, Dr. Matas reported on intralaryngeal insufflation [30] and states, "Until the danger of seriously interfering with the respiratory functions by inducing acute collapse of the lung is clearly eliminated or is reduced to a safe minimum, the analogy between the pleura and the peritoneum from the surgical point of view will never exist."

In a talk on Surgery of the Chest before the Louisiana State Medical Society published in the *Transactions of the Louisiana State Medical Society* in May, 1898,[31] Dr. Matas emphasized the value of the Fell-O'Dwyer apparatus as a method of preventing and overcoming the effects of acute traumatic thorax in thoracic operations. In a presentation before the American Surgical Association in May, 1901,[31] he states:

About this time [1897] I received a copy of the Medical and Surgical Reports of the Presbyterian Hospital in New York for 1896 which contained a brief but excellent article by Dr. Northrup in which he demonstrated the value of the Fell-O'Dwyer apparatus as an aid to artificial respiration in the treatment of opium narcosis and other surgical conditions. Too much credit cannot be given Dr. Northrup for his persistent advocacy of this valuable apparatus, the invention of his lamented and ingenious colleague, O'Dwyer. The reading of this article together with the repeated demonstration of its unfailing and almost marvelous efficiency in cases of opium narcosis in the hands of Dr. J. D. Bloom, surgeon in charge of Charity Hospital at New Orleans, immediately suggested to my mind that this was the apparatus needed in thoracic surgery.

The suggestion grew upon me and it was my confidence in its value that led me to take it as the basis for an address before the Surgical Section of the Louisiana State Medical Society in May, 1898. Since then, the clinical confirmation of the value of the principle of intralaryngeal insufflation in overcoming collapse of the lung following upon resection of the chest walls has been amply confirmed by my colleague, Dr. F. W. Parham, whose able and exhaustive monograph on "The Surgical Treatment of Tumors of the Chest Walls" is familiar to all of those who have followed the latest developments in this field of thoracic surgery. The interesting case just reported by our distinguished Fellow, Dr. Keen, also illustrates the practice of pulmonary insufflation to overcome a collapse of the lung in traumatic pneumothorax, but the form of the apparatus used, that is, the Fell mask by which air is insufflated by the oronasal method, is liable to failure, chiefly from the dropping of the tongue backward and introduction of air into the pharynx instead of the air passages and is therefore unreliable as a surgical method, more especially in critical conditions in which certainty and precision are absolutely necessary; that in this case (Dr. Keen) the collapse of the lung which followed the entrance of air into the pleura would have been promptly overcome if an intralaryngeal cannula had been used as in Dr. Parham's case cannot be doubted. The recovery of of the patient and the absence of untoward symptoms when the pleura was opened simply illustrate the fact that in this, as in other recorded cases, acute surgical pneumothorax does not invariably cause an arrest in the respiration in both lungs; but in man, more often than in dogs and other low animals, there is often a tolerance to the invasion of

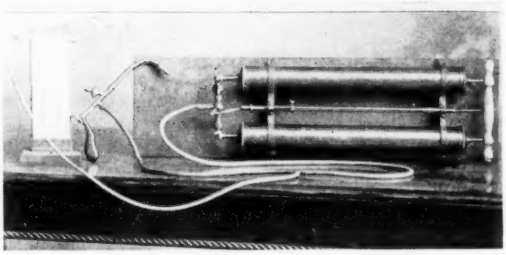


Fig. 19.—Original Matas illustration of experimental pump for artificial respiration. "Experimental automatic respiratory apparatus with double inspiratory and expiratory cylinders." (From Matas,[31] *Transactions of the American Surgical Association,* Philadelphia, J. B. Lippincott Company.)

the pleura with air, provided the air is allowed to enter and fill the pleura gradually. This toleration of pulmonary collapse in some cases does not argue that the occurrence of this condition is free from peril; on the contrary, the numerous cases which have been recorded only confirm the experimental evidence which conclusively demonstrates that the sudden admission of air in the pleura through a large fenestrum is one of the greatest danger elements in intrathoracic surgery and one of the most serious obstacles in the advancement of surgery of the chest.

Dr. Matas together with Dr. John Smythe then worked with various apparatuses to produce the proper pulmonary insufflation. They showed that the bellows apparatus which was used in the Fell-O'Dwyer technique was not adequate. They first devised a pump with two cylinders, one which exerted positive pressure and one which exerted negative pressure (Fig. 19). They found, however, that animals did poorly when this apparatus was used, because damage to the bronchioles and alveoli was caused by the negative pressure during the expiration.

After demonstrating to our satisfaction that the double inspiratory and expiratory pump was not a practical appliance for artificial respiration, we abandoned the aspirating cylinder entirely in our work and utilized the single insufflating cylinder on the O'Dwyer principle and have found it perfectly reliable and have made it the basis of our practical clinical respiratory machine [Fig. 20].

They even connected to the apparatus a funnel through which chloroform might be administered to the patient who was being treated.

Dr. Matas early became interested in local and regional analgesia. He was the first in America to use spinal analgesia. On Nov. 19, 1899, he anesthetized a patient by "the spinal subarachnoid method," using β-eucaine, but the anesthesia was unsatisfactory.

One month later, on December 18, 1899, I renewed the attempt with cocaine using one cc. of one per cent solution repeated in five minutes injecting it between the third and fourth lumbar spaces. The result was extraordinary, not only complete anesthesia of the body below the waist but it gradually extended to the neck and head to a lesser degree but sufficiently to pinch and puncture the skin of the

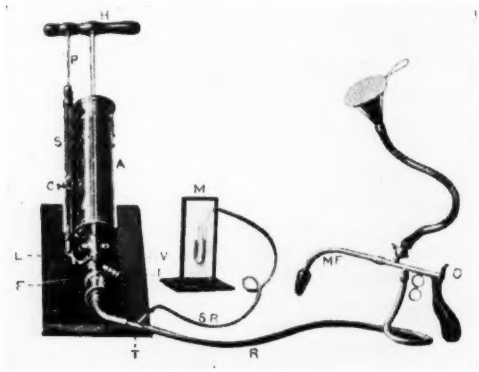


Fig. 20 (continuation of Fig. 19).—"Latest working model of apparatus for artificial respiration in medical and surgical practice." (From Matas,[31] *Transactions of the American Surgical Association,* Philadelphia, J. B. Lippincott Company.)

face and neck without pain. No untoward or alarming symptoms occurred during the operation and the patient recovered but then, the usual reactions followed: chills, nausea, vomiting, a rise in temperature. This, I believe, was the first published operation that was performed under spinal anesthesia in this country with the difference of only a few days of a case reported by J. B. Murphy in Chicago which followed. I then continued to use cocaine but never exceeded the height of the second lumbar vertebra. The results from the purely analgesic viewpoint were admirable in anesthetizing all the regions below the waist but the chills, headache, vomiting, and febrile rise which occurred so frequently made me doubtful of its advantage over a general narcosis with ether. I was about to publish my experience with the first 50 cases when a series of accidents in the last three, one an abdominal hysterectomy for fibroid, in which the patient was saved only by persistent efforts at artificial respiration; another, a hyperpyrexia with a temperature of over 104°F., and a third with an intense rachialgia and headache that persisted for months—made me realize that the dangers of spinal anesthesia with cocaine could not possibly be compensated by the simplicity of the technique or the effectiveness of the anesthesia, so much so, that I, in company with many other pioneers, abandoned it altogether until novocaine was introduced by Braun in 1905-1906.

Fig. 21.—Original Matas illustration of apparatus for local anesthesia infiltration. "Apparatus for rapid, massive infiltration anesthesia. Charging the cylinder with air-pump." (From Matas,[36] *Transactions of the American Surgical Association,* Philadelphia, J. B. Lippincott Company.)

Dr. Matas did considerable investigative work in the anatomical laboratory to determine the method and site of injection in spinal analgesia.[35] His intensive training as an anatomist was of great value in this respect. In 1900, he reported seven cases of spinal analgesia in which cocaine was used and described a method of regional block. In speaking of regional block for operations on the upper extremity in which he injected the three nerves, muscular spiral, median, and ulnar at the bend of the elbow, he states:

> The possibility of this method suggested itself to me in 1897 but no opportunity presented itself for its application until January, 1898 when an old man, age 76, applied to my clinic for the relief of an extensive and deep epitheliomatous ulcer which involved a large portion of the dorsal and hyperthenar regions of the right hand.

The operation was apparently very successful.

Dr. Matas devised an apparatus for infiltrative anesthesia.[36] His original apparatus consisted of a graduated nursing bottle and a pump. Because he had difficulty with the bottle breaking, particularly when he injected the anesthetic into an indurated area, he devised a metal cylinder which could stand considerable pressure.[36] Air would be forced into the cylinder, after which the cylinder would be inverted, with the anesthetic solution below, and by means of a control valve he could control the anesthetic agent (Figs. 21 and 22). Dr. Matas suggested a method of anesthesia of the second division of the trigeminal nerve by injecting it at the foramen rotundum. He was able to remove both the maxillae of a patient with carcinoma with this type of anesthesia on April 29, 1899.[32]

In addition to his many other firsts, he was the first to differentiate between typhoid fever and malaria in Louisiana.[37] Other excellent articles which Dr. Matas has written are "Beriberi," published in 1883,[38] which was written after his stay in Cuba as an

interpreter for the Yellow Fever Commission, and "Iliac Phlegmons," an excellent anatomic and surgical discussion, in which the development of infections undoubtedly following appendicitis are described.[39] He also published articles on "The Treatment of Fractures of the Jaw" || and "The Treatment of Fractures of the Zygomatic Arch and of the Lower Jaw." In 1925 he published an excellent historical résumé on yellow fever, entitled "A Yellow Fever Retrospect and Prospect." [42]

As illustrated by the various operations which he described and by the apparatuses which he devised, it is obvious that Dr. Matas has a great amount of ingenuity. This was further illustrated in an operative procedure which was the first operation that I saw Dr. Matas perform. In January, 1927, while I was visiting New Orleans in order to "be looked over" as a possible successor to Dr. Matas, I saw him perform one of the most unusual operations that I have ever seen. The patient was a middle-aged woman with extensive neurofibromatoses with one extremely large tumor originating from the posterior part of the trunk, which actually weighed more than the patient herself did. As can easily be imagined, it was no easy feat to try to cope with such a situation, but this presented no difficulty for Dr. Matas. The day before the operation he arranged for a block and tackle to be suspended from the ceiling of the operating room. He sterilized a pair of ordinary ice tongs, and, after the patient had been anesthetized and placed in the prone position, the sterile ice tongs were thrust into the tumor and, by means of the block and tackle, the tumor was elevated away from the patient's body. In order to control bleeding, Wyeth pins were placed through the base of the tumor and on the proximal side of the Wyeth pins a tourniquet was tightly applied. In this way it was relatively easy to separate the patient from the tumor, with a minimal amount of bleeding. There are few surgeons who would have had the imagination and ingenuity to have devised such a means of handling such a difficult problem.

Fig. 22 (continuation of Fig. 21).—"Cylinder charged and inverted. The pumping outfit is detached when the apparatus is in operation." (From Matas,[36] *Transactions of the American Surgical Association,* Philadelphia, J. B. Lippincott Company.)

In addition to being a great surgeon and a pioneer in many fields of surgery, particularly vascular surgery, Dr. Matas has one of the finest minds anyone has ever had. He has a phenomenal memory, and it is indeed a treat to listen to him give a discussion even though he may not have had time to prepare for it. I know of no person who is able to speak extemporaneously so fluently, and so authoritatively, as he can (Figs. 23 and 24). He is cultured and can discuss fluently matters pertaining to literature, art, and music. He is also inter-

|| References 40 and 41.

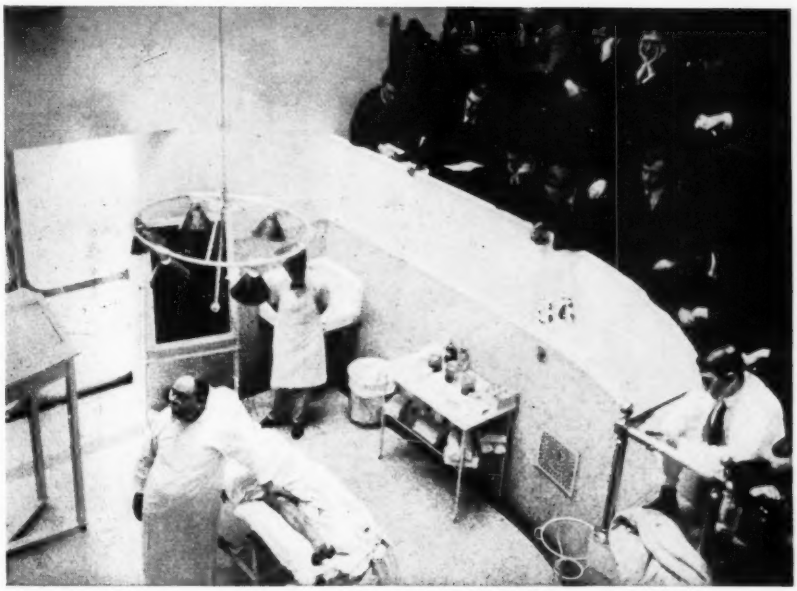


Fig. 23.—Dr. Matas demonstrating popliteal aneurysm to Tulane Medical students in the original Miles Amphitheater, Charity Hospital, New Orleans, 1917. (Courtesy of Dr. Mims Gage.)

ested in sports and at one time attended movie theaters fairly frequently. He has always emphasized the value of motion pictures in research and teaching and as early as 1912 wrote an article on "The Cinematograph as an Aid to Education and Research."

Dr. Matas is an indefatigable worker (Figs. 25, 26, and 27). He spends long hours in his library, and his former house officers tell me that it was not unusual, when he was active in practice, for him to insist that he be informed of a particular patient's progress at regular times during the night, when apparently he would be working, regardless of the time of the night. He is an extremely kind person and, as can be imagined, is

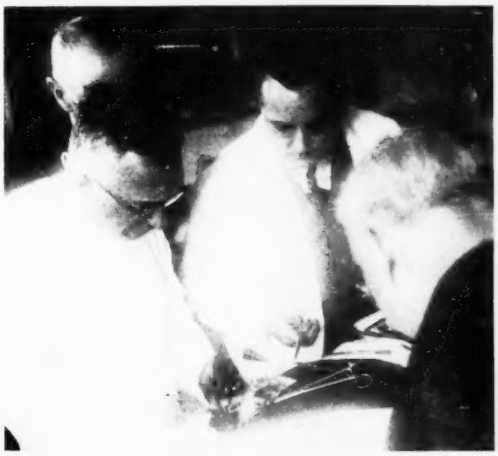


Fig. 24.— Photograph of Dr. Matas (with his back to the camera), Professor Nystrom, and Dr. George Lilly, President of the Society for Vascular Surgery, at the time of Professor Nystrom's visit to New Orleans. Professor Nystrom is demonstrating the technique of pulmonary embolectomy.

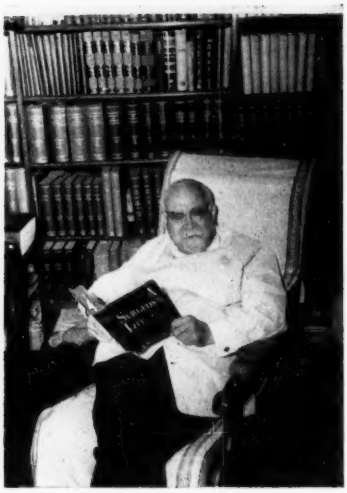


Fig. 25.—Dr. Matas in library in his home.

greatly beloved by all. Dr. Matas is a man of great integrity. One of the finest articles that has ever been written is his "Soul of a Surgeon," which he presented as the annual oration at the 48th Annual Session of the Mississippi State Medical Association, in May, 1915. In speaking of the medical student who faints when he sees his first operation, he states:

> The youth who feels deeply and struggles at his first surgical experience shows that he is normal, that he is psychically and physiologically sound, he shows that he has feelings, that he has imagination, that he has pity, and that he has a human quality that will make him a humane surgeon, he is a man who will worry and who will, through his very sensibility, feel most keenly the burden of his responsibility when it will be his turn to be a leader and a master. It is all wrong for people to believe that the sight of blood is indifferent to the surgeon. On the contrary, the older and more experienced he is, the more anxious he is to conserve it, and to see as little of it as possible, in the course of his operation. Every real surgeon is happy when he can speak of his bloodless operation, and he is miserable when he has to admit that he has spilled much of it in an unavoidably bloody one.
>
> Gentleness, compassion, tenderness do not exclude firmness. Persuasiveness and authority may travel hand in hand. Neither are resoluteness and an inflexible will incompatible with an inexhaustible patience and genuine sympathy.

Dr. Matas was one of the 12 founders of the American College of Surgeons in 1913. He was its president in 1925-1926, and he received an honorary fellowship in the American College of Surgeons in 1952. He was president of the American Surgical Association in 1909. He was also president of the International Society of Surgery in 1936, president of the American Association for Thoracic Surgery in 1920, president of the Southern Surgical and Gynecological Association in 1910, and received the first Certificate of Merit awarded by the American Medical Association. He is a member of practically every surgical association in the world and has been an honorary member of most of them. He is an honorary member of the Real Academia Medicina of Barcelona, the Royal College of Surgeons (England), the French Association of Surgery, National Cuban Order of Carlos Finlay, Order of

Fig. 26.—Dr. Matas in library in his home, the largest private medical library in New Orleans.

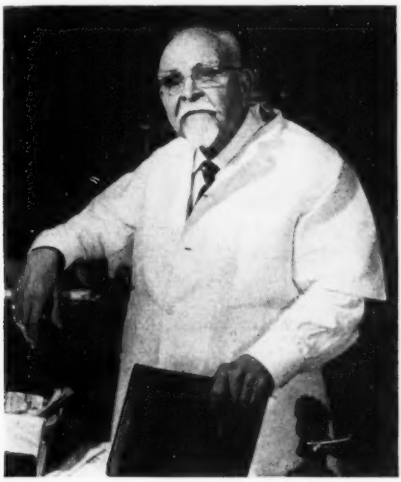


Fig. 27.—Recent photograph of Dr. Matas.

Leopold of Belgium, Gorgas Medical Society, Havana Academy of Medicine, and Spanish Royal Academy (Fig. 28). He received the Henry Jacob Bigelow Medal, in 1926, and has received honorary degrees from his alma mater, Tulane University, Princeton University, Washington University, the University of Pennsylvania, the University of Alabama, and the National University of Guatemala. He also received the Times-Picayune Loving Cup as the outstanding citizen of New Orleans in 1940. Dr. Matas has written voluminously and has published more than 300 articles. For many years he has been working on a History of Medicine in Louisiana, which in reality is a history of Louisiana. It is a gigantic project and, when finished, will comprise 16 volumes (Fig. 29).

There is probably no other person who has accomplished as much in his span of life as Dr. Matas has, and it has given me a great deal of satisfaction and pleasure to pay tribute to this splendid humanitarian, brilliant scholar, and eminent scientist and surgeon, who has done so much to further vascular surgery. The greatest tribute I have ever had paid me was when I was chosen

Fig. 29.—Drs. Matas and Grey Turner during meeting of International Society of Surgery in New Orleans, in October, 1949.

Fig. 28.—Dr. Matas receiving jewel of Commandership of Order of Carlos Finlay at New Orleans at 25th Convention of International Association of Lions Clubs, July 22-25, 1941.

to succeed Dr. Matas as Professor of Surgery at Tulane University. No one realizes better than I that to succeed Dr. Matas is impossible, but I can assure you that to follow in his footsteps and to be stimulated by his tremendous accomplishments have been real stimuli to me in my endeavors. I sincerely hope that those of you who have not been fortunate enough to know him have obtained some idea of the person whom we all love and revere.

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Significance of the Induced Digital Vasoconstrictive Reflexes

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Digital vasoconstrictive responses to sensory stimulation have been known for many years; however, they have not been considered useful diagnostic signs of disease of the nervous system or blood vessels, since the many factors influencing these reactions have not been adequately clarified.* It is the purpose of this report to examine the nature of the induced vasomotor reflexes and to point out certain conditions in which knowledge of the behavior of these reflexes is of clinical value.

METHODS AND MATERIALS

Approximately 500 induced vasomotor reflexes have been studied in 125 persons. Forty-five subjects were normal; 45 had organic arterial disease due to arteriosclerosis; 20 were blind or deaf subjects without vascular disease; 10 had Raynaud's syndrome, and 5 had emotional problems resulting in strong anxiety states. The average age was 39 years, with a range of 20 to 62. Sixty per cent were female. Vasodilatation was induced by having the patients rest in a comfortable, warm environment with a room temperature of 25 ± 1 C.[4] The vasomotor reflexes were studied with a sensitive electronic digital pneumoplethysmograph.† A digital cup was sealed to the fingertip or toetip, and volume changes were recorded by means of a heat stylus or ink-writing recorder. The instrument was standardized so that a 10 mm. rise of the stylus represented a 10 cu. mm. increase in volume of the part. In one group of studies an ankle cuff exerting 300 mm. of air pressure was employed instead of the digital cup to record the volume change at the ankle. The instrument was standardized for this technique so that a 10 mm. upward deflection of the stylus represented a 100 cu. mm. volume increase of the part. Respirations were recorded by placing the temperature-sensitive element of a Thermistor Thermometer ‡ in a nostril and graphing the temperature changes of the inspired and expired air.[7] Expiration resulted in a rise of the stylus because of heating of the Thermistor, and inspiration resulted in a fall of the stylus because of cooling of the Thermistor. Venous pressure was recorded with a strain gauge.§ Various stimuli (such as light, sound, touch, and pain) were used to produce sensory stimulation in order to produce vasomotor responses. Inspiration (deep breath) also produced digital vasoconstriction.

RESULTS

Vasoconstrictive responses to the various stimuli employed showed certain similarities. The magnitude of the responses varied roughly with the intensity of the stimulus. Vasoconstriction commenced three to four seconds after administration of a stimulus and lasted one-half minute to two minutes. When the subjects were undergoing vasodilation, the pulse waves were high (for fingers, 6 to 12 cu. mm. per beat). During maximum vasoconstriction the pulse waves were low (less than 2 cu. mm. per beat).

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From the Nash Cardiovascular Research Foundation, Hospital of the Good Samaritan; Department of Medicine, University of Southern California School of Medicine, and the Department of Biophysics, University of California at Los Angeles.

* References 1 to 3.

† References 5 and 6.

‡ Electro-Medical Engineering Company, Burbank, Calif.

§ Model P23B 0 to 5 cm. Hg. Statham Laboratories, Los Angeles.

TABLE 1.—*Stimuli Which Produce Digital Vasoconstriction*

Inspiration
Expiration
Pain
Anxiety
Startle by light, sound, or touch
Tickle
Cold
Electric shock
Cerebration, for example, mathematical calculation or observation of a Rorschach card

Various stimuli were employed (Table 1). Inspiration (deep breath) was a convenient means of producing vasoconstriction and was used for routine testing. A pinwheel on the skin, which produced pain, was easily administered and produced a large response. Anxiety, in certain persons, produced intense vasoconstriction of long duration. Startle by light, sound, or touch was a satisfactory stimulus if not repeated too often, since accommodation took place with these stimuli in certain persons. Electric shock produced a prompt, intense response which could be accurately timed. Vasoconstriction to this stimulus was of long duration, possibly because of anxiety which was associated with this procedure. Cerebration—for example, mathematical calculation—produced vasoconstriction in many persons. These vasoconstrictive responses were inhibited by the agents and procedures shown in Table 2.

Typical vasoconstrictive responses to inspiration are shown in Figure 1. In normal subjects the volume decrease of the digit averaged 40 cu. mm. and the duration averaged 45 seconds (Fig. 1, *A*). Reinforced inspiratory reflexes were produced often by two successive inspirations, which resulted in W-shaped curves with large volume decreases of long duration (Fig. 1, *B*). Prolonged constrictive responses were seen commonly in patients with anxiety states (Fig. 1, *C*). Absence of inspiratory reflexes occurred characteristically after a sympathectomy (Fig. 1, *D*). Paradoxical responses occurred after sympathectomies, often as a result of the mechanical effects of breath-holding (Fig. 1, *E*).

The magnitude of the inspiratory reflex was studied in 40 patients with organic arterial disease before and after sympathectomy (removal of ganglia L-2 and L-3). The magnitude of the response varied with the amount of organic arterial disease which was present (Fig. 2). These patients were divided into four groups on the basis of the magnitude of the inspiratory reflexes. Groups I, II, III, and IV showed large, medium, small, and absent reflexes, in that order. Group I: Ten patients had minimal organic arterial disease. In this group all had intermittent claudication on walking more than two blocks at a rate of about 2 miles per hour. Peripheral pulses were diminished but not absent. There were no demonstrable tissue changes. Plethysmograms of the toes after vasodilatation were abnormal in seven cases because of low amplitude of pulsations or low blood flow as

TABLE 2.—*Effects of Drugs and Procedures on the Induced Vasoconstrictor Reflexes*

Drugs *		
Which Inhibited the Reflexes	Which Did Not Inhibit the Reflexes	Procedures Which Inhibited the Reflexes *
Hexamethonium (4)	Alcohol (1, 2, 7)	Decrease in sensitivity of a sensory organ, for example, local procaine in the skin (1)
Pentolinium (4)	Neostigmine (7)	Blocking vasomotor center with an organic lesion (2)
Tetraethylammonium (4)	Pentobarbital (1)	Block of sympathetic system at the level of ganglia surgically (4)
DH alkaloids of ergot (2, 6)	Histamine (7)	Block of a peripheral sensory nerve, for example, posterior tibial nerve block (5)
Tolazoline (6, 7)	Glyceryl trinitrate (7)	
Ecolid (SU3088) (4)	Carbonol (7)	
Pendiomide (1, 4)		
Hydralazine (2)		
Hydergine (1, 2, 6)		
Reserpine (1, 2)		
Dibenzaline (6)		
Chlorpromazine (6)		

* The numbers in parentheses refer to these sites of action: 1, afferent pathways from sensory organ or cerebral cortex to vasomotor center; 2, subcortical regions, probably vasomotor center; 3, spinal cord; 4, sympathetic ganglia; 5, peripheral nerve trunk; 6, neuroeffector organ between nerve and artery; 7, direct action on artery.

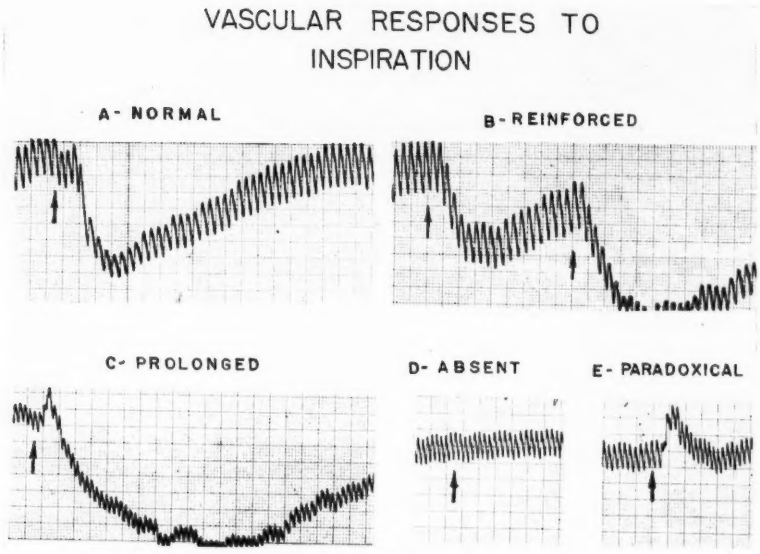


Fig. 1.—Five types of vascular responses to inspiration are shown. The paper speed is 2.5 mm. per second. The arrow indicates the time of onset of inspiration.

shown by the venous congestion test. In these patients a large vasoconstrictive reflex, averaging 35 cu. mm. in magnitude, was found. Lumbar sympathectomy gave excellent results in all 10 patients, as shown by increases in skin temperatures, dilatation of veins, and improved nutrition of the skin. Group II: Ten patients had moderate organic arterial disease. This group was characterized by intermittent claudication upon walking one block. They were without dorsalis pedis and posterior tibial pulses and had abnormal plethysmograms. There was no significant amount of tissue atrophy. The reflexes averaged 15 cu. mm. In eight patients in this group lumbar sympathectomy

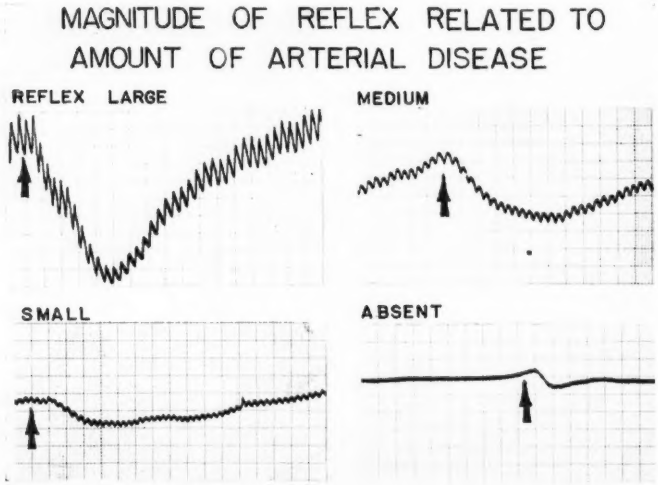


Fig. 2.—Examples of large, medium, small, and absent vasoconstrictive responses following inspiration among patients with minimal arterial disease (Group I), moderate arterial disease (Group II), severe arterial disease (Group III), and far-advanced arterial disease (Group IV). Patients with minimal arterial disease had large vasoconstrictive responses whereas those with far-advanced arterial disease had little or no vasoconstrictive responses. The time of onset of inspiration is shown by the arrow.

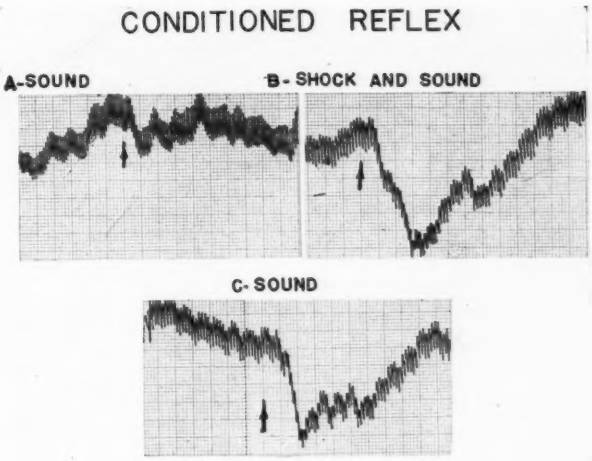


Fig. 3.—The conditioned reflex to sound is shown in one patient. *A*, a nonirritating soft buzzer failed to produce a significant amount of vasoconstriction. *B*, a painful shock with the sound produced a large vasoconstriction. These stimuli were administered for from 20 to 40 times. *C*, the sound alone resulted in a large vasoconstriction because of conditioning. The stimuli were applied at the arrows.

produced good (but not excellent) clinical responses, as shown by improved nutrition of the skin and other findings. The remaining two patients obtained excellent results. Group III: Ten patients had advanced organic arterial disease and experienced intermittent claudication on walking one-half block. All had atrophy of the tissues of the toes. None had night pain or pain on elevation of the legs to 45 degrees for three minutes. The magnitude of the vasoconstrictive responses to inspiration of this group averaged 8 cu. mm. In these patients lumbar sympathectomy produced only minimal clinical improvement. Group IV: Ten patients with far-advanced disease also were studied. Most had night pain or pain on elevating the legs, and all had advanced tissue changes. The reflexes of this group were usually absent or generally less than 3 cu. mm. In nine patients there was no significant improvement in the peripheral circulation after lumbar sympathectomy, as judged clinically, and in one patient gangrene of a toe developed four days after surgery.

Conditioning of the reflex was attempted in 10 patients by using electric shock and sound (Fig. 3). A soft nonirritating buzzer which failed to produce vasoconstriction of the finger was used. An electric shock was then administered which produced pain and a large vasoconstrictive response. Conditioning of the vasoconstrictive response was accomplished by administering the shock and buzzer together for from 20 to 40 times. After this period, the buzzer alone was sounded, resulting in a large vasoconstriction. This indicated that conditioning of the vasoconstrictive response had occurred to the stimulus which previously failed to produce a vasoconstrictive response. This response was blocked by different agents or procedures which acted on portions of the reflex pathway (Table 2).

The ability to block voluntarily the normal vasoconstriction to sound or light was studied in 10 normal, 10 blind, and 10 deaf subjects (Fig. 4). A 100-watt white lamp placed 3 ft. from the subject was employed as a stimulus in the blind studies. The light shined in the eyes of the blind subjects failed to produce vasoconstriction. The subjects whose vision was normal had large vasoconstrictive responses when the light was shined in the eyes. The normal subjects then were instructed to resist seeing the light. Large vasoconstrictive responses again resulted, in spite of the attempts to resist. Similar results were found in deaf subjects when a sound was used as a stimulus.

Accommodation to a sound repeated 5 to 50 times was studied in five patients. The stimulus employed was a loud buzzer placed

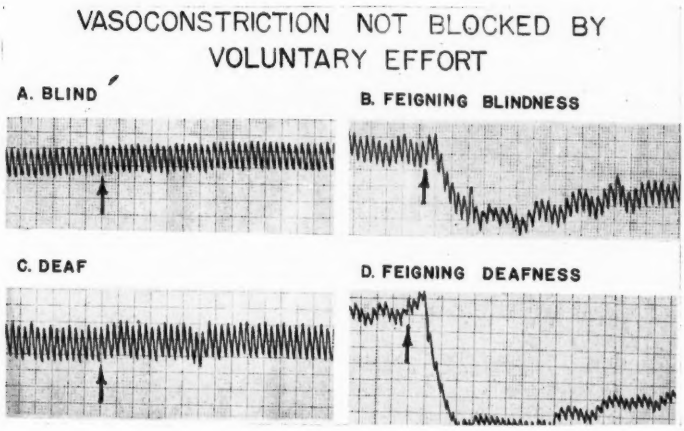
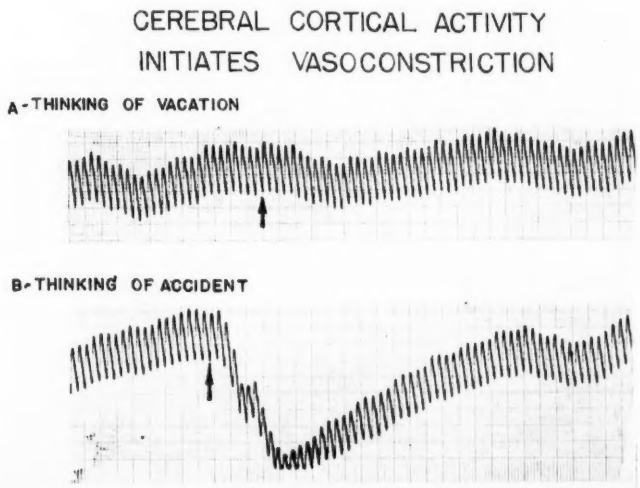


Fig. 4.—Subjects with normal sight and hearing were unable to block voluntarily the vasoconstrictive responses induced by light or sound; however, blind and deaf subjects showed no responses to these stimuli. *A*, a light shined in the eye of a blind patient produced no vasoconstriction. *B*, a light shined in the eye of a normal subject who resisted vasoconstriction voluntarily showed the presence of vasoconstrictive responses in spite of the effort to resist. *C*, a sound stimulus in a deaf person showed no vasoconstriction. *D*, a normal subject voluntarily resisting vasoconstriction showed constrictive responses to sound in spite of the effort to resist. The times at which the stimuli are applied are shown by arrows.

3 ft. from the ear. In four of the patients the magnitude of the vasoconstrictive responses became less with repeated stimulation until finally no constriction occurred. One patient failed to accommodate although the stimulus was sounded 50 times. In this patient the response would occur some of the time. It was thought that this irregular response might be due to inhibiting stimuli which were occurring periodically.

The role of the cerebral cortex in the production of vasoconstrictive responses was

Fig. 5.—Cerebral cortical initiation of vasconstriction is shown in one patient. *A*, thinking of a vacation produced no vasoconstriction. *B*, thinking of an auto accident in which the patient was involved resulted in vasoconstriction.



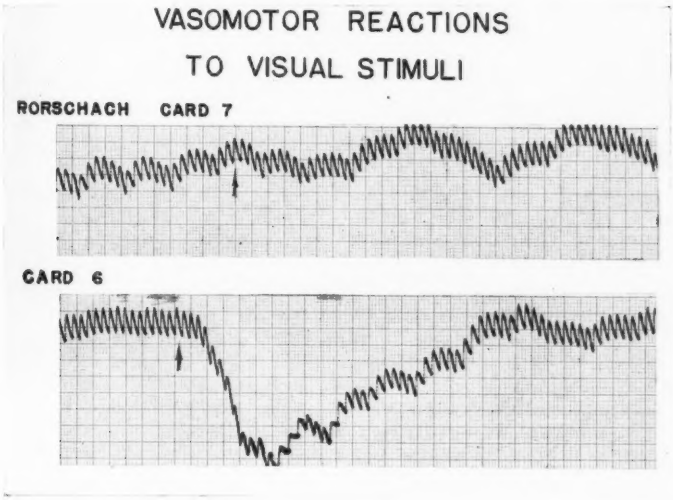
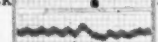
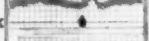


Fig. 6.—The effect of the interpretation of environmental situations on vasomotor reactions is illustrated by the records of one patient shown. Rorschach Card 7 failed to produce vasoconstriction of the finger. Card 6 resulted in vasoconstriction of the finger. Card 7 reminded the patient of a tranquilizing situation. Card 6 reminded the patient of a disturbing situation.

studied in 20 patients. Thoughts of tranquilizing situations (for example, a pleasant, relaxing vacation) produced little if any vasoconstriction in these patients, while thinking of disturbing situations (for example, a severe accident) usually produced vasoconstriction (Fig. 5). The importance of the subject's interpretation of environmental situations was studied in 16 of these patients by employing the standard Rorschach cards as stimuli (Fig. 6). Various cards were placed before the subjects,

Fig. 7.—The reflex arc resulting in vasoconstriction of the vessels of a digit is subcortical, because a painful stimulus failed to produce vasoconstriction after CCK 179 injection, procaine spinal block, hexamethonium injection, procaine block of a peripheral nerve, and tolazoline (Priscoline) injection; however, the reflex was present after pentobarbital.

PAIN ACTIVATES SUBCORTICAL REFLEX ARC PRODUCING VASOCONSTRICTION

SITE OF ACTION OF DRUG	DRUG	PAINFUL STIMULUS AT BLACK ARROW	VASOCONSTRICTIVE REFLEX
CORTEX	PENTOBARBITAL		PRESENT
MEDULLA	CCK 179		ABSENT
CORD	PROCAINE BLOCK		ABSENT
SYMP. GANGLIA	C6		ABSENT
PERIPHERAL NERVE	PROCAINE BLOCK		ABSENT
EFFECTOR ORGAN	PRISCOLINE		ABSENT

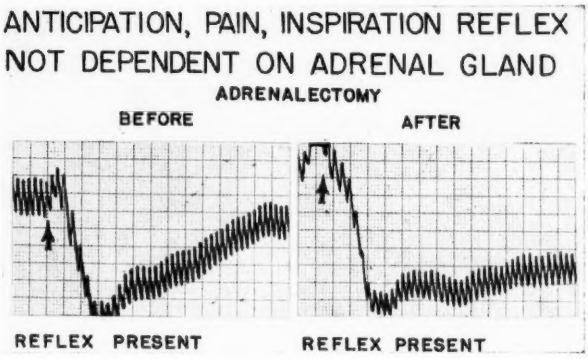


Fig. 8.—Sensory stimulation and inspiration produced vasoconstriction before and after adrenalectomy.

and the vasomotor reactions were recorded. Vasoconstriction took place with certain cards more frequently than with others. The results of one patient are shown in Figure 6. Card 7 failed to produce a vasoconstrictive response, whereas Card 6 produced a vasoconstrictive response of moderately long duration. The patient stated that Card 6 reminded him of an unpleasant situation, whereas Card 7 was not unpleasant. The results in the entire group were irregular; however, eight of the patients showed different vascular responses to the test cards employed.

The influence of various drugs and procedures on the induced vasoconstrictive reflexes was studied in 55 patients. The results are summarized in Table 2, which show the drugs and procedures employed along with probable sites of action. The strongest inhibiting agents were the ganglionic blocking agents, which in adequate dosage appeared to block completely the sympathetic impulses to the vessels, since the inspiratory reflexes were abolished. Sympathetic ganglionectomy (removal of L-2 and L-3) usually removed most, but occasionally not all, of the vasoconstrictive responses, since the induced re-

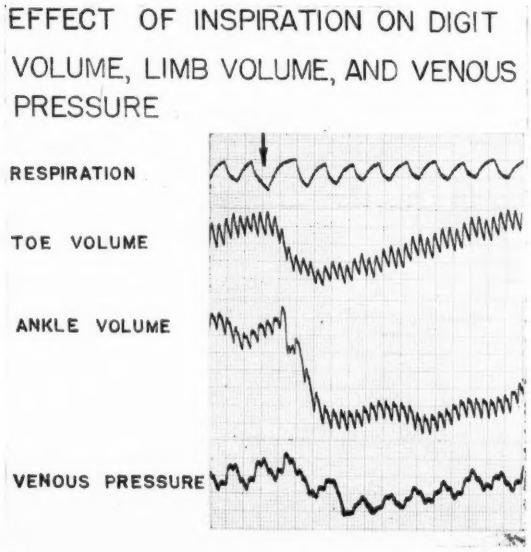


Fig. 9.—Inspiration resulted in a decrease in volume of the toe and ankle and a decrease in venous pressure.

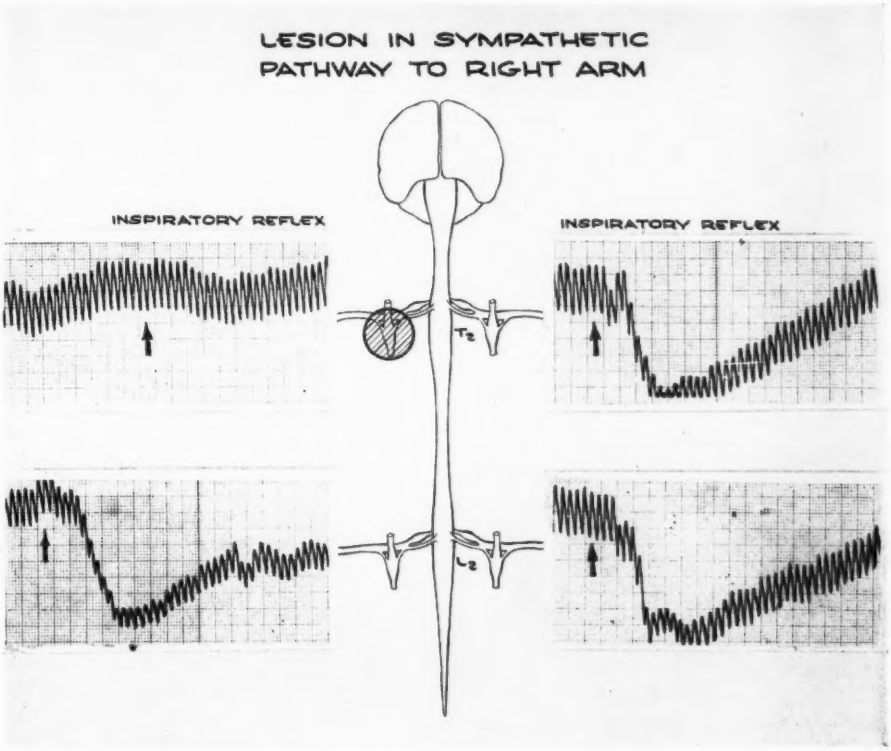


Fig. 10.—A lesion destroying the right second thoracic ganglion resulted in an absence of the vasoconstrictive responses in the right finger following inspiration, whereas vasoconstriction occurred in the digits of the other limbs, whose sympathetic nerve supply was intact.

flexes were present at times after this procedure (see below).

The reflex arc which results in vasoconstriction of the digit following painful stimulation of the skin was studied in four patients (Fig. 7). Various agents were employed on different occasions which provided a pharmacologic block of the reflexes at various points in the reflex arc. The reflex was absent after tolazoline (Priscoline) hydrochloride, a posterior tribial nerve block with procaine, hexamethonium, a spinal anesthetic with procaine, and the DH alkaloids of ergot. The respective sites of action of these agents are at the effector organ, the peripheral nerve, the sympathetic ganglion, the spinal cord, and the medulla.‖ The reflexes were not blocked by 0.3 gm. (4.5 grains) of pentobarbital intravenously. This drug acts at the level of the cortex; thus, the reflex arc would appear to be from the sensory organ to the subcortical region of the brain through the sympathetic nervous system to the blood vessels.

The reflexes induced by anticipation, pain, and inspiration were studied in three patients before and after adrenalectomy (Fig. 8). In all, the reflexes were present before surgery and were unmodified by the adrenalectomy.

The simultaneous determinations of toe volume, ankle volume, and antecubital venous pressure were carried out to determine if inspiration resulted in vasoconstriction of the vessels of the ankles as well as those of the toes and to determine the effects of inspiration and other stimuli on antecubital

‖ References 8 and 9.

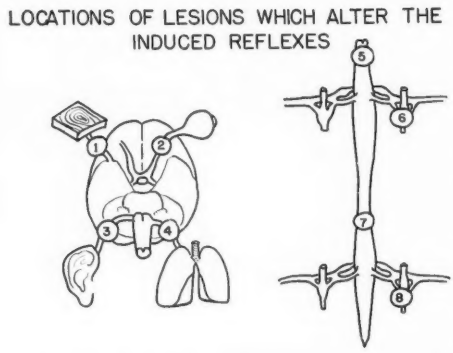


Fig. 11.—Lesions in various sensory organs or in various portions of the nervous system altered vasomotor reactions in one or all of the extremities.

venous pressure. Eight patients were studied (Fig. 9). Inspiration resulted in a decrease in toe and ankle volume and venous pressure. In five patients this test was repeated with a blood pressure cuff which was inflated to 70 mm. of mercury and which was placed on the upper arm between the needle in the antecubital vein and the heart. This was employed in order to occlude venous return and to prevent venous pressure changes from occurring as a result of the mechanical sucking action of the chest associated with inspiration. In these patients there was an average increase in venous pressure of 25 mm. of water with inspiration.

An attempt to demonstrate lesions in the sympathetic nervous system employing the inspiratory reflex was made in 21 patients. Reflexes were recorded from the index finger of each hand and the second toe of each foot. An example of a patient with a lesion in the right second thoracic ganglion is shown in Figure 10. Following inspiration the vasoconstrictive responses in the right index finger were absent, whereas they were present in the other digits. Lesions of the sensory organs or nervous system resulted in the following patterns: 1. Afferent sensory nerve lesions blocked vasoconstrictive responses in all four extremities when light, sound, or pain were employed as a stimulus but did not block the vasoconstriction associated with inspiration (Fig. 11, Structures 1, 2, and 3). 2. Brain stem lesions blocked the vasoconstrictive reactions when sound, pain, light, or inspiration was employed as a stimulus (Fig. 11, Structure 5). 3. Upper thoracic sympathetic ganglionic lesions showed absence of vasoconstriction on the ipsilateral arm with preservation of constrictive reaction in the other three limbs (Fig. 11, Structure 6). 4. Middle spinal cord lesions resulted in reflexes which were present in fingers but diminished or absent in toes (Fig. 11, Structure 7). 5. Lumbar sympathetic ganglionic lesions blocked reflexes in the ipsilateral leg but did not affect reflexes in the other limbs Fig. 11, Structure 8).

The completeness of a lumbar sympathectomy was studied in 20 patients before and one to two months after a conventional (L-2, L-3) sympathectomy. In 80% the reflex was absent after surgery, and in 20%

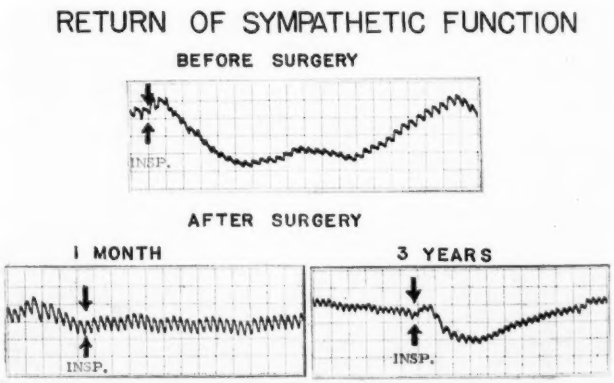


Fig. 12.—A return of sympathetic function is likely if the induced vasomotor reflexes are absent one month after surgery but are present some years after surgery. Incomplete removal of sympathetic nerves is likely when the vasoconstrictive reflexes are present after as well as before sympathectomy.

the reflex was present but small. Fifteen of these patients were studied for return of sympathetic function. This was done by recording the reflexes one month and again one to three years after surgery. In only one of these patients had a definite return of function taken place (Fig. 12).

The possibility of producing vasoconstrictive conditioned reflexes and later blocking these reflexes with vasoinhibiting or vasodilating conditioned reflexes was explored in 10 patients. In order to demonstrate changes in vasomotor tone, plethysmograms were recorded with a special technique which permitted changes in the height of the pulsations of the digits without recording the slower volume changes of the digit. The procedure employed was as follows: A dim yellow light was turned on and off repeatedly until no vasoconstrictive response occurred. Next, a loud, irritating buzzer which produced constriction was sounded simultaneously with the yellow light, which produced vasoconstriction. These stimuli were repeated together until conditioning had taken place and the patients responded to the yellow light alone by vasoconstriction. Next, a blue light only was turned on periodically and the patient was encouraged to relax, thus producing vasodilatation. This was repeated until conditioning had occurred so that the blue light alone produced vasodilatation. In this way two conditioned reflexes were established, one a stimulating or constricting reflex produced by the yellow light and the other an inhibiting or dilating reflex produced by the blue light. An attempt to inhibit vasoconstriction produced by the yellow light was carried out as follows: The yellow light was turned on, resulting in vasoconstriction in most patients (Fig. 13). While the yellow light was still on and during the period of vasoconstriction, the blue light was turned on. This resulted in vasodilatation in four of the patients. On the turning off of the blue light, leaving only the yellow light, vasoconstriction occurred, as the yellow or constricting stimulus was still present. The yellow light was then turned off, and vasodilatation occurred. Of the group studied, inhibition of the conditioned vasoconstrictive reflex was accomplished in four.

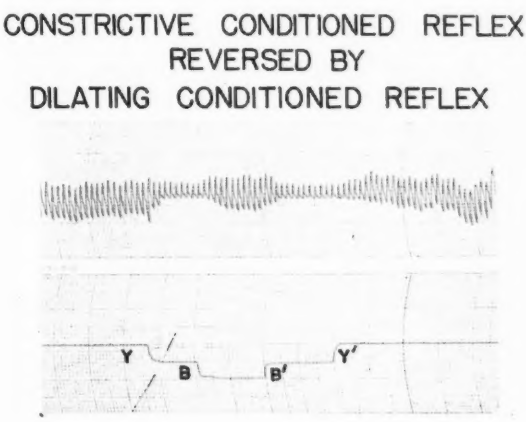


Fig. 13.—Conditioned vasoconstrictive reflexes of a finger were temporarily inhibted by conditioned dilating reflexes. At *Y* a yellow light was turned on and remained on until *Y'*. At *B* a blue light was turned on and was turned off at *B'*. At *Y* the height of the pulse waves decreased. At *B* the pulse amplitude increased. At *B'* the pulse waves decreased, and at *Y'* they increased. See text for explanation.

COMMENT

Vasoconstrictor reflexes at the finger, toe, or ankle may be induced by various stimuli, such as a deep breath (inspiration), anxiety, sensory stimulation, or cerebration. The reflexes behave characteristically and may be classified as normal, prolonged, absent, or paradoxical. They may be reinforced by using the same stimulus twice in rapid succession or by using two different stimuli at one time. Accommodation to certain stimuli

occurs, and conditioned responses develop readily. The magnitude and character of the reflex is modified by disease of sensory organs, brain, sympathetic system, or blood vessels. The response ranges from reflexes of large magnitude which occur with normal pathways and blood vessels, to absence of reflexes resulting from advanced organic disease. The magnitude of the response before surgery may be correlated with the degree of success of a lumbar sympathectomy. Patients with large vasoconstrictive responses preoperatively had excellent results from sympathectomy, whereas those with small or absent responses preoperatively had poor or harmful results. The constrictive responses to a startling light or sound could not be willfully blocked; however, constriction or relaxation of vessels could be brought about in some subjects by thinking of disturbing or tranquilizing situations. For example, thoughts of pleasant, relaxing situations resulted in vasodilatation, and exciting, stimulating, or unpleasant thoughts produced vasoconstriction. Also, the interpretation of environmental situations resulted in vasoconstriction or vasodilatation. For example, two persons looking at a single Rorschach card may show different vascular responses. One subject, who is reminded of a tranquilizing situation, dilates; the other subject, who is reminded of a disturbing situation, constricts.

The reflex arc over which impulses travel after sensory stimulation, such as a pinwheel on the skin, appears to be from the sensory organ, over the afferent nerve to subcortical regions of the brain, and with efferent pathways over the sympathetic nervous system to the peripheral blood vessels. The reflex arc is probably subcortical, as large doses of pentobarbital failed to obliterate the vasoconstrictive responses to pain. The induced vasomotor responses are apparently associated with venous constriction, as a rise in venous pressure following an inspiration can be demonstrated when a venous tourniquet has been placed between the needle in the antecubital vein and the heart. In this way the venous pressure variations caused by the mechanical sucking action of the expanding chest are inhibited or eliminated, and the changes in venous pressure which occur probably are the results of changes in venomotor tone mediated by way of the sympathetic nervous system.

Knowledge of the behavior of the induced reflexes can be of practical value. By recording the reflexes at a digit of each appendage, it is possible to identify the approximate location of lesions in sensory organs, brain stem, sympathetic ganglia, spinal cord, or peripheral nerves. The completeness of a sympathectomy can be estimated by demonstrating the presence or absence of the inspiratory reflexes after surgery. If the reflexes are completely unchanged from those recorded preoperatively, sympathetic nerves probably have not been removed. If the reflexes are small, probably only a portion of the sympathetic nerves has been removed. With a complete sympathectomy, the reflexes characteristically are absent. The measurement of skin resistance also aids in demonstrating the effects of sympathectomy.[10] The return of sympathetic function can be estimated by determining the presence or absence of the induced reflexes one month after sympathectomy and again one year after sympathectomy. Return of sympathetic function is suspected when the reflexes are small or absent one month after surgery but are large one year after surgery.

These studies have demonstrated that it was possible to condition easily vasoconstrictive or vasodilatnig reflexes. Also, it was possible to reverse the constrictive reflex by administering a dilating stimulus while the constrictive stimulus was still present. This suggests that it is possible through the process of conditioning to promote vascular relaxation and inhibit vasoconstriction. It is probable that therapy based on these principles would be of value in patients with Raynaud's disease as well as patients with other disease states.

SUMMARY

The induced sympathetic vasoconstrictive reflexes may be employed to assist in the demonstration of lesions of the sympathetic system, to determine the completeness of a sympathectomy, and to detect the return of sympathetic function after sympathectomy. It has been shown that conditioned vasoconstrictive reflexes can be reversed by substituting conditioned inhibiting (vasodilating) reflexes. This principle may have therapeutic value.

Mrs. Grayce Fleming provided technical assistance in this study.

These studies were carried out through grants from the Los Angeles Heart Association and the Heart Research Foundation, Los Angeles.

DISCUSSION

DR. ROBERT GOETZ, Capetown, South Africa: I was very interested in Dr. Winsor's paper because it deals with phenomena which we all have seen. All those who have done plethysmography have recorded constrictor reflexes occurring with deep inspiration or spontaneously. I should like to ask Dr. Winsor whether he noticed any relation of these spontaneous or induced constrictor reflexes with changes in the posture of the limb and whether the vessels were first fully dilated in those tracings which he showed us.

One other question comes to mind in relation to the tracing demonstrating a return of reflexes following sympathectomy. Was it in an upper or a lower limb in which that occurred?

Our experience with sympathectomy in the lower limb is such that we can confidently say that return of vasoconstrictor tone practically never occurs unless the sympathectomy has not been complete in the first place. In the upper limb this is not the case, even if the sympathectomy was originally anatomically complete, particularly if the operation has been a preganglionic sympathectomy in contrast to a ganglionectomy. We believe that these reflexes recur after a certain lapse of time on account of a reorganization in the sympathetic chain.

DR. TRAVIS WINSOR, Los Angeles: In answer to Dr. Goetz' comments:

Answer 1.: All studies were made with the patients supine and the digits near heart level (half the anteroposterior diameter of the chest). With the patients in this position the toes were near heart level without further positioning. The fingers were elevated to this level by placing supports under the hands.

Answer 2: The vasomotor tone of the patients studied was intermediate (vessels dilated partially), which was accomplished by making studies in a comfortably warm environment with the patients covered with one light blanket. With the vessels in this state either vasodilatation or vasoconstriction could be detected.

Answer 3: We found a return of sympathetic function in the lower extremities in a small group of 40 patients one year after surgery, as shown by the presence of inspiratory reflexes at this time. These patients were examined one month after surgery, and sympathetic function could not be demonstrated (inspiratory reflexes absent). A return of sympathetic function occurred in a higher percentage of patients at one year in the upper extremities.

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Lumbar Sympathectomy for Arteriosclerosis

Status of One Hundred Patients Five Years After Operation

EDWARD A. EDWARDS, M.D.
and
CHILTON CRANE, M.D., Boston

INTRODUCTION

In 1950 we analyzed the results of lumbar sympathectomy in 100 patients suffering from arteriosclerosis of the lower limbs.[1] It appears desirable to analyze the results again, since the follow-up period at the time of the initial report was short, averaging 20 months.

We may briefly review the material previously presented. The group probably comprised a fair sample of the disease. Twenty-seven of the patients were diabetic. There were 79 men and 21 women. Their ages varied from 34 to 82, with the majority in the upper age groups. Serious disease in the vital organs, especially the heart, was noted in 39. The major limb arteries showed moderate or severe occlusion in all patients.

There were two postoperative deaths and six thigh amputations within the first eight weeks. A seventh thigh amputation was performed on one of the patients who died.

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Associate Clinical Professor of Anatomy, Harvard Medical School; Associate in Surgery, Peter Bent Brigham Hospital (Dr. Edwards). Associate in Surgery, Harvard Medical School; Senior Associate in Surgery, Peter Bent Brigham Hospital (Dr. Crane).

The five-year status will be considered under the categories of patient survival, limb survival, and condition of the limbs.

PATIENT SURVIVAL

Thirty-five patients have died (Fig. 1). Coronary heart disease was the cause of death in 22; various other causes were responsible in the remainder. To the two who died postoperatively were added eight more in the first year. Somewhat fewer deaths occurred in each of the succeeding four years. Death or survival could be related to the presence of diabetes, the pattern of the local process, and the response to sympathectomy.

TABLE 1.—*Unfavorable Results After Sympathectomy*

	Diabetic (27)	Nondiabetic (73)	Total (100)
Deaths in 5 yr.	15 (55.6%)	20 (27.4%)	35%
Poor postoperative condition of limb	8 (29.6%)	7 (9.6%)	15%
Thigh amputations (included in above)	6 (22.2%)	4 (5.5%)	10%

Diabetes was the only general factor which appeared certainly to have a bearing on death (Table 1). There was no correlation between death and age at time of operation, and only a questionably positive correlation with the female sex and with prior existence of severe visceral disease.

The pattern of the local disease prior to sympathectomy bore some relation to death or survival. Among those who died, the antecedent process in the limb had been more rapid in onset and in progression, the majority having had symptoms for less than six months, and the local condition most frequently being based on arterial thrombosis. Necrosis or threatened necrosis, rather than claudication, had been the presenting symp-

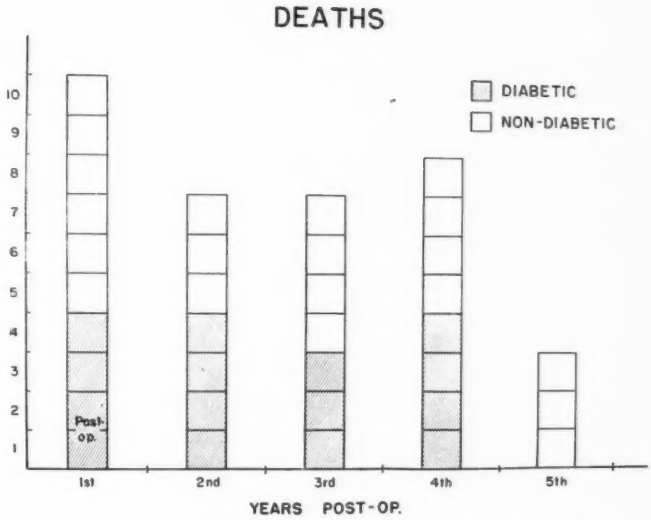

Fig. 1.—Deaths in the five-year postoperative period.

tom more frequently in those who died than in the survivors. The previous loss of the contralateral limb offered a bad prognosis, five of the nine patients in this category succumbing in the first five postoperative years. The pulse level could not be related to survival.

The third positive factor was the response to sympathectomy. Of the 15 patients whose result was poor, 10 died in the five-year period. Of the 10 amputees (included in the category of poor response), 7 died; of the 5 who lost both limbs after sympathectomy or the limb remaining after a prior amputation, 4 died.

LIMB SURVIVAL

In addition to the seven thigh amputations performed in the early postoperative period, three more were done during the first year. Thereafter no major amputations proved necessary (Fig. 2). Transmetatarsal and toe

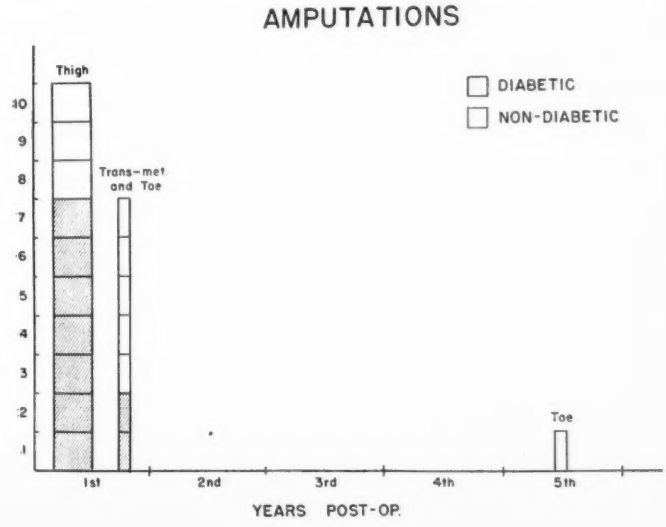

Fig. 2.—Amputations in the five-year postoperative period.

amputations were done on seven patients the first year, and one was done in the fifth year.

The need for major amputation could be definitely correlated with diabetes and with impending death. Patients coming to major amputation constituted 22.2% of the diabetic group and 5.5% of the nondiabetic group. It is only fair to point out that a greater proportion of the diabetics operated on had limbs which were in a desperate condition. There was an excessive number of amputations on those who were to die in the five postoperative years (Table 2). There was no correlation with age or sex.

Correlations between the need for major amputation and local factors were considered in our previous report but may be mentioned again. Most amputations were necessary in patients having an over-all deterioration of the limb rather than a localized necrosis. The good outcome after the minor amputations emphasizes this point. Deep necrosis of the foot or leg, on the contrary, did lead to major amputation.

TABLE 2.—*Incidence of Amputations After Sympathectomy*

Amputation	5 Yr. Survivors (65)	Patients Dead Within 5 Yr. (35)
Thigh	3 (4.6%)	7 (20%)
Double (included in above)	1 (1.5%)	4 (11%)
Transmetatarsal or toe	7 (10.7%)	1 (3%)

Previous loss of the contralateral limb was an ominous beginning: Four of the nine patients in this category lost the second limb, and five of the nine died within the five year period.

POSTSYMPATHECTOMY CONDITION OF THE LIMB

A word about definitions. We can all agree that thigh amputation or persistent pain necessitating a chair existence should be classified as a poor result. The group we have called good includes patients who are working comfortably or, if superannuated, are comfortably performing that amount of exercise expected of patients at their age. Claudication was rarely completely overcome, even in the good category, but it was considerably improved in almost all these cases.* Patients whose result was called fair were those who were pain-free on moderate restriction of activity.

The condition of the treated limbs was considered in the surviving group, and while the patients were alive in those who died in the five years (Fig. 3). In the majority of both groups the results were good. A greater proportion of poor results was associated with early death, 28.6% in those who died as against 7.7% in the survivors. As in other considerations, diabetes exerted an adverse effect; the results were poor in 29.6% of all the diabetics, as against 9.6% of the nondiabetics.

The same correlations held regarding the local problem in the limb as for amputations, i. e., patients did better when the problem was claudication or a localized superficial necrosis and worse when gangrene of the entire foot threatened. The presence, prior to sympathectomy, of a single pedal pulse, however weak, was always followed by a good local result.[1] A good result was usually maintained throughout the period of observation. A few patients developed later occlusions of the major arteries at a level higher than that with which they originally presented, yet even in these cases severer claudication, rather than gangrene, was the outcome.

The condition of the contralateral limb when the original problem and the operation were unilateral is of interest in deciding on a policy of one-sided or two-sided operative treatment at the outset. In 63 of our patients unilateral operation had been performed. Subsequent sympathectomy, defined as done six months or more after the first operation, was performed in eight of these patients. Two patients of our entire series came to thigh amputation on the side not originally operated on; one of these had had a subsequent sympathectomy preceding the

* Our general experience is that about 75% of patients operated on obtain substantial improvement of claudication.

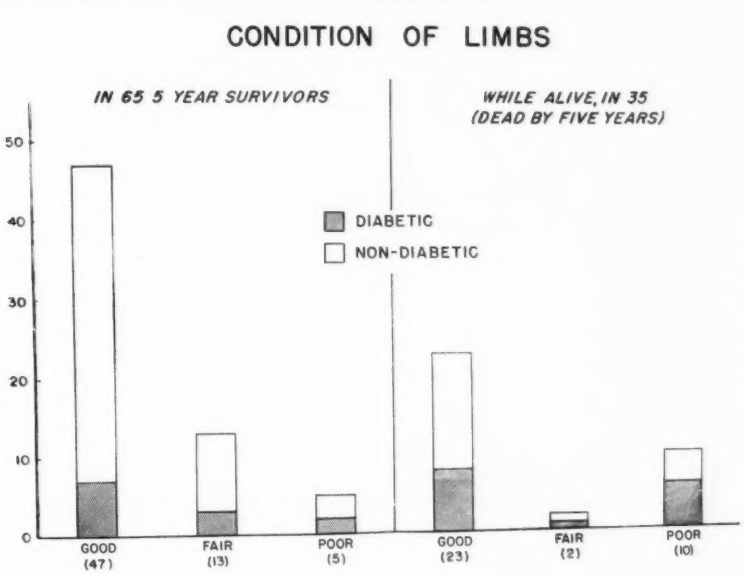

Fig. 3.—Condition of the limbs after operation in the five-year postoperative period. The poor results include all major amputations.

amputation. We know of a third patient who came to contralateral amputation six years after sympathectomy.

COMMENT

Our amputation rate and death rate are both lower than that reported by Berry, Flotte, and Coller [2] and by Pratt [3] in two larger series followed for shorter periods of time. It would seem that such disparity in results reported after sympathectomy reflects a difference in philosophies as to the choice of patients for operation. Under one philosophy the operation is tried only when all other measures have failed and gangrene is imminent. The results following this plan will be extremely poor. In a second, sympathectomy is used as the major therapeutic effort in almost all active patients who show symptoms of arteriosclerosis in the lower limbs. Here the results will be almost uniformly good. A third, and our current philosophy, lies somewhere between the two. We emphasize the conservative value of the operation for chronic ischemia, but we also perform it for fairly sick limbs when we believe the procedure has a fair chance of success.[4]

Amputations were necessary three times as frequently in Pratt's diabetic patients as in his nondiabetic ones, but Berry, Flotte, and Coller found the results essentially the same in the two groups. The latter authors observed, as we have, that poor local results, and especially amputations, are associated with a high death rate. Our observations also agree that a short preoperative history is associated with a higher amputation and death rate.

We regard the desirability of performing a bilateral operation, at one or two sessions, when the original ischemia is unilateral as debatable. Only 3 (if we include the six-year case) of our 63 patients with a unilateral sympathectomy subsequently lost a limb. A unilateral operation is decided on either because the contralateral limb has minimal or no signs of ischemia, or because the patient's general condition is poor, making double jeopardy seem unsafe. We apply this rule less rigidly to our younger and more active patients, for whom life expectancy is longer and the chances for further trouble therefore greater. Careful follow-up will usually avert difficulty in patients who have had unilateral operation. Our policy is never to discharge the arteriosclerotic

patient permanently. We advise sympathectomy for the contralateral limb if any signs of vascular deterioration develop, taking note particularly of the development of claudication, murmurs over the major artery of the limb, or a lowering of oscillometric reading. It is probable that contralateral amputation could have been prevented in two of our three cases if they had returned frequently for examination.

SUMMARY AND CONCLUSIONS

The status of 100 patients with arteriosclerosis of the lower limbs, 27 of whom were diabetic, was determined five years after lumbar sympathectomy.

Sixty-five patients have survived. Death in the others was due mostly to coronary heart disease. Factors predisposing to death were the presence of diabetes, a rapid progression of the arteriosclerosis in the limb prior to operation, and a limb problem of over-all ischemia rather than localized necrosis.

The results in the limbs of the majority of patients were good. More poor results occurred in those who died than in the survivors and in the diabetics than in the nondiabetics.

Once the major difficulties of the first few months are past, the limb is usually safe. This would seem to indicate that the favorable effects of lumbar sympathectomy are retained.

A picture emerges of two types of arteriosclerotic patients. One with a relatively localized arterial involvement of slow progression responds well to sympathectomy and has a good life expectancy. The other has a diffuse arterial involvement of rapid progression, does poorly after sympathectomy, and has a poor life expectancy.

DISCUSSION

DR. ROBERT BERRY, Ann Arbor, Mich.: I should like to congratulate Dr. Edwards on his excellent presentation and his number of good results.

During the period 1945-1948 we attempted to establish criteria for lumbar sympathectomy by performing the operation in almost everyone with symptomatic arteriosclerotic peripheral vascular disease who obviously did not need amputation. Undoubtedly, many useless sympathectomies were done and these poor results have been reflected in our statistics. Since our second review in 1954, the indications for sympathectomy have been sharply narrowed (*Surgery* **37**:115-129, 1955).

However, we do not make a case against diabetes as enthusiastically as the essayist. When we compared the results in 80 diabetics and 80 nondiabetics who developed ulceration, gangrene, or a combination of both, little difference was found in the amputation rate, life expectancy, or the number of good results from sympathectomy. Furthermore, little influence was observed because of adequacy of treatment, duration of disease, or length of time that the patient had had diabetes. These results tend to confirm the observations of E. T. Bell, who did about 1500 autopsies on diabetics and was unable to correlate the above factors with longevity of the patient. Perhaps it is necessary to define the type of diabetic we are talking about. The diabetes that develops in 60- to 70-year-old persons appears to be more benign that the type having onset prior to 35 years of age.

DR. ROBERT GOETZ, Capetown: Our experience is very much like that of Dr. Edwards. We also have had poor results in our diabetic patients. However, there is one point which in the past has been overlooked and which we think is important in this respect. Many cases of diabetes, particularly if they have any degree of neuritis, provide evidence that some or all of the peripheral sympathetic fibers are already interrupted. We have tested many of these patients and found that peripheral vasodilation cannot be induced by ablating sympathetic tone. These are the cases in which sympathectomy will fail. We are, therefore, very strict in the selection of diabetic patients, and we believe that it is essential to demonstrate preoperatively a response of the collateral vessels to vasodilator procedures.

Sympathectomy is not contraindicated in complete occlusion of the main vessels, provided one can demonstrate a response of the collateral vessels to the ablation of sympathetic tone by whatever method used, such as the Gibbon and Landis test, vasodilator drugs, or sympathetic block. The case with the high arterial occlusion responds, in our experience, better than the one in which the peripheral vessels are involved. This can probably be explained by the fact that, if the small peripheral vessels are occluded, the collateral circulation cannot develop as well as in the case of a high occlusion, in which the collateral blood flow often reenters the main stream and the circulation carries on in the main vessels.

I was interested in your point whether one should do a bilateral sympathectomy in one session. Originally, I believed that, because sympathectomy is such an easy operation, why not operate on both legs while the patient is under the anesthetic. We

did so for years and found that our results following bilateral sympathectomy were not as good in the leg with advanced disease if the other leg had a moderate involvement only. If in the one leg the circulation is near normal and in the other very much advanced, unilateral sympathectomy is the better procedure because we avert the shunting of blood into the better leg due to the greater reduction in peripheral resistance produced by the sympathectomy in the better leg.

DR. JOSEPHUS C. LUKE, Montreal, Canada: May I present an observation of ours concerning one group of patients included in the series presented by Dr. Edwards. This is the group with calf claudication and little in the way of trophic ischemic changes in the foot. In doing arteriograms on this type of case, frequently we find femoral occlusion in the region of the adductor canal with no evidence of patent distal main vessels. However, a good collateral circulation is demonstrated. Grafting procedures are out of the question, but the results of sympathectomy have been pleasingly surprising in the marked improvement in claudication distance. We have observed a sufficient number of these postoperative cases that in similar levels of occlusion we can promise the patient an increase to double or quadruple his former claudication distances.

If sympathectomy is done when the occlusion is high in the superficial femoral artery, the patient therefore receiving almost his entire distal blood flow via the profunda femoris branch, claudication distance is rarely improved. A sympathectomy in such a case will bring about warming of the foot but will not relieve the symptoms complained of, resulting in a disgruntled patient.

DR. KEITH S. GRIMSON, Durham, N. C.: I'd like to ask Dr. Edwards to enlarge for a moment on one point in his paper and that is the incidence of gangrene following sympathectomy, if it is a significant feature. I gained the impression that it was in a certain group of patients. We have not been plagued by this development, having had only two evident or obvious developments of gangrene in an extremity following sympathectomy, and, in one of those in which we were permitted a good examination and did it, we found that the reason for the bad outcome in the extremity was a spontaneous arterial thrombosis, widely distributed through the limb. In that patient we found from the operative record that a fall in BP had occurred during the operation. We would correlate the gangrene with the fall in BP and thrombosis rather than with the sympathectomy per se. Perhaps Dr. Edwards can help with this problem.

DR. EDWARD A. EDWARDS, Boston: I hesitate to close without additional comment on the diabetic problem. Statistical inferences drawn from a group as small as ours may be faulty. The relatively poor results in our diabetics may be due in part to the generally severer illness of the diabetic and in part to the fact that at the outset we operated on diabetic patients only when their circulatory status was quite desperate. At present, while we recognize that results are not likely to be as good in the diabetic, we nevertheless operate on diabetic patients with some eagerness because of their great need.

Dr. Goetz mentioned that neuritis may itself obviate sympathetic function. This may be true to a limited extent. On the other hand, the cold sweating that often accompanies neuritis suggests that sympathetic irritation is at least as frequent, and neuritis should, therefore, constitute no contraindication to sympathectomy.

Dr. Grimson has brought up the problem of gangrene after sympathectomy. We have had this unfortunate outcome in several instances. In our experience two different types of mechanism may be responsible. The first is arterial or venous thrombosis developing at or immediately after operation. The reality of this pathology has been demonstrated by dissection of the amputated limbs. The second mechanism is the combination of vasoconstriction and fall in pressure which Dr. Grimson has brought up. Probably these factors can produce gangrene only in limbs whose circulation is already desperately poor. Preoperatively the patient has usually been hanging the limb down to obtain hydrostatic aid for his blood flow. On the operating table, this aid is denied. Meanwhile, the anesthesia may cause a fall in blood pressure as well as peripheral vasoconstriction. Additional constriction may be produced by operative handling of the sympathetic trunk, as O'Keeffe, Warren, and Hill (*S. Forum* [1950] pp. 391-394, 1951) have shown. When the blood flow is critically reduced, the red cells begin to agglutinate in the terminal vessels and gangrene follows. We pay a good deal of attention to the prevention of a fall in pressure at operation. In the recovery room the head of the bed is elevated as soon as possible to again obtain the aid of hydrostatic pressure, and in instances of severe ischemia we give heparin starting within three or four hours after operation.

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Spinal Cord Lesions Produced by Aortography in Dogs

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Aortography, venography, and angiocardiography are generally accepted as valuable diagnostic procedures. Aortography is often employed for aortic or peripheral arterial vascular disease and for investigation of the arteries supplying the kidneys and other abdominal organs and tumors. Many contrast media have been used since the early report of use of sodium iodide for arteriography by Dos Santos, Lamas, and Pereira,[1] in 1929. Melick, Byrne, and Boler [2] in 1952 compared several iodine compounds and found sodium iodide more toxic than iodopyracet (Diodrast). They considered sodium acetrizoate (Urokon Sodium) least toxic. Sodium acetrizoate is commonly used in a 70% solution for aortography and in a 35% solution for femoral arteriography or for venography. Iodopyracet is generally recommended in a somewhat less concentrated solution. The few serious complications which have occurred with aortography have been caused by injury of organs which receive their blood supply directly from the lower aorta.

Paraplegia and death of one patient were reported by Antoni and Lindgren in 1949 [3] following aortography using an unspecified contrast medium. Autopsy revealed necrosis of the spinal cord. Boyarsky, in 1954,[4] reported paraplegia and survival of one patient following aortography using 15 cc. of 70% sodium acetrizoate. This patient had a complete motor and sensory loss below the level of the eighth thoracic segment but later recovered from the sensory loss and regained bladder and partial motor function. The aortic puncture in each of these two patients was made at the level of the first or second lumbar vertebra. A fatality caused by mesenteric thrombosis was reported by Wagner and Price in 1950.[5] It occurred in one patient of a series of 50 undergoing abdominal aortography. Ten cubic centimeters of 80% sodium iodide had been injected into the superior mesenteric artery. Serious renal complications were reported by Miller, Wylie, and Hinman, in 1954,[6] as occurring in 7 of 250 patients who had aortography using 50 to 100 cc. of 70% iodopyracet. In three unilateral renal damage followed infusion of the dye predominantly into one renal artery; in four a reversible bilateral renal failure occurred.

Undoubtedly other injuries to the spinal cord, mesenteric circulation, or kidneys have occurred. Rogers * has told us of a total paraplegia following a retrograde aortogram with injection of first 20 cc. and then 30 cc. of 70% sodium acetrizoate at the level of the 12th thoracic vertebra. Others have told us of one or two unreported injuries of each type. In our first 43 aortograms with one

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* Rogers, L. S., personal communication.

or two injections of 50 cc. of 70% acetrizoate, one patient without aortic obstruction had a temporary renal suppression, and another with complete aortic obstruction below the renal arteries had extensive renal necrosis and died.

It would seem that a serious complication might occur as frequently as one among each 50 patients studied by aortography, an incidence and severity of trouble much higher than that following use of the same contrast medium given intravenously. The more serious complications of aortography seem to relate directly to a high concentration of the radiopaque material at the origin of the mesenteric, renal, and spinal arteries; they also may relate to abnormalities of blood flow and to individual sensitivity of the organs supplied. Any of the iodine contrast media can cause tissue damage. An occasional comment in the References and the actual observation in one of our two instances of renal damage suggest that an abrupt elevation of blood pressure and slowing of heart rate during the intra-aortic injection of a dye should be considered as a warning of impending damage.

The present study was designed to deliberately produce spinal cord injury in dogs and to observe roentgenological, anatomical, and histopathological alterations. Sodium acetrizoate † and iodopyracet ‡ were selected as the contrast media because of their general clinical use and because reports indicate that these chemicals are least toxic.

METHOD

Experiments were carried out using adult dogs weighing between 15 and 42 lb. Operations were performed using pentobarbital sodium for anesthesia and sterile technique. The abdominal cavity or the left thoracic cavity was opened to visualize the aorta. The animal was in a supine position when injections were made into the abdominal aorta and was on its right side when injections were made into the thoracic aorta. The contrast medium was injected through an 18-gauge needle inserted obliquely, upward, or cephalad into the aorta. Three sites of injection were selected. The first was a point in the abdominal aorta just below the origin of the renal arteries (Fig. 1*A*). The second was a point in the abdominal aorta a few centimeters

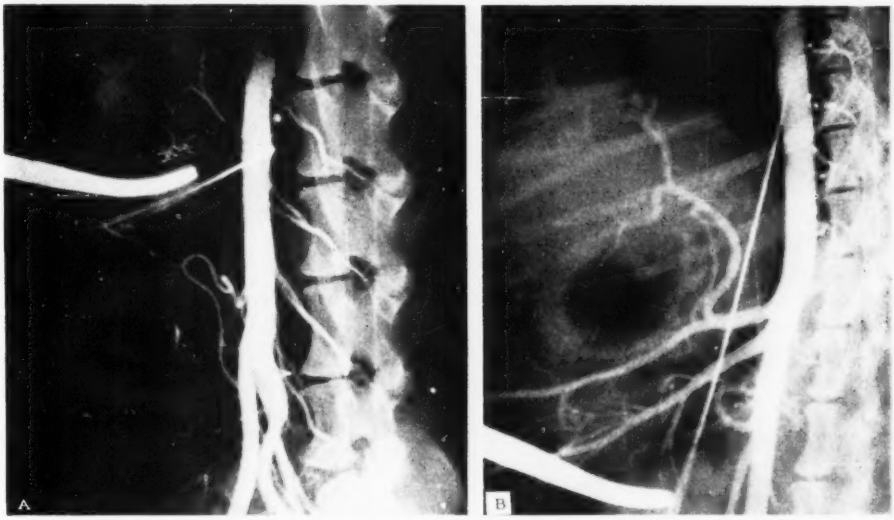

Fig. 1.—Two sites of puncture of the aorta of dogs are illustrated by the aortograms. *A*, below the renal arteries; *B*, above the superior mesenteric. The forceful injections of the contrast medium have caused retrograde filling of 3 or 4 cm. of the aorta above the point of insertion of the needles.

† Supplied as Urokon Sodium by Mallinckrodt Chemical Works, St. Louis.

‡ Supplied as Diodrast by Winthrop-Stearns, Inc., New York.

above the origin of the superior mesenteric artery (Fig. 1*B*). The third was the midthoracic aorta. The volume of contrast medium was 7 cc. in some experiments and 15 or 20 cc. in others. Injections were made forcibly, using manual pressure on the syringe. Time of injection varied from 5 to 10 seconds. After injection the incisions were closed, and the dogs were allowed to recover. Each animal was observed constantly for several hours and then daily until killed for autopsy. A record was kept of all reactions of the dogs, the degree of any convulsion during injection, and the type and extent of any paralysis which developed afterward. At intervals of from several hours to 34 days the animals were killed. Pathologic examinations were carried out by one of us (G. M.). Details of these

TABLE 1.—*Intra-Aortic Injections, Fifteen Cubic Centimeters of Sodium Acetrizoate or Iodopyracet, Below Renal Arteries*

	Sodium Acetrizoate, 70%	Iodopyracet, 70%
Iodine content	65.8%	49.8%
No. of dogs	6	6
No. with paraplegia	6	2
Level of spinal cord lesion		
Lumbosacral	2	3
Thoracolumbar	2	0
Thoracolumbar and sacral	2	0
Grade of injury, spinal cord		
++++	4	0
+++	2	0
++	0	1
+	0	2

studies are presented elsewhere.[7] In 14 dogs the anatomy of the arterial circulation of the spinal cord was mapped by one of us (A. K. T.). The vessels were observed under a dissecting microscope.

EXPERIMENTAL RESULTS

Control Experiments. — Control experiments were made in two groups of four dogs each, administering volumes of 15 cc. of sodium acetrizoate intravenously in one group and into the periaortic areolar tissue through an abdominal incision in another group. Six dogs placed in a prone position received translumbar injections of 15 cc. into the upper abdominal aorta. These control procedures did not produce any recognizable abnormalities of function.

After preliminary trials had determined that 15 cc. of sodium acetrizoate injected through an aortic puncture site just below the renal arteries would produce paraplegia in supine dogs, a comparison was made between 70% sodium acetrizoate and 70% iodopyracet. Dogs of similar weight were paired and on each of six days one of each pair was injected with 15 cc. of sodium acetrizoate, the other with 15 cc. of iodopyracet. Results are indicated in Table 1. It is noted that the iodine content of sodium acetrizoate, 65.8%, is 32% more than that of iodopyracet, 49.8%. Each of the six dogs receiving sodium acetrizoate developed spastic paraplegia. Two of the dogs receiving iodopyracet developed paraplegia. Another developed slight weakness of the legs, and three had no demonstrable abnormality. The degree of injury of the spinal cord was severer with the sodium acetrizoate.§ No lesion was demonstrable in the spinal cords of three of the animals which had been given iodopyracet. The remaining experiments were performed with 70% sodium acetrizoate because of the consistency with which the lesion of the spinal cord could be produced.

Effects of Injections at Different Levels.— Injections at a Point Below Renal Arteries: Injections of 15 cc. were given through a straight No. 18 needle in five dogs; injections of 20 cc., through a straight needle in three, and injections of 15 cc., through a needle with a curved point to direct the dye toward the anterior wall of the aorta, in four. Results are summarized in Table 2. All dogs in each group had a severe extensor rigor or spinal convulsion immediately after the injection and subsequently developed spastic paraplegia or, in one animal, spastic paraparesis. The spinal cord lesion as determined by autopsy was located in the lumbosacral and coccygeal region in each dog. No significant differences occurred with use of 15 or 20 cc. volumes or with use of straight or curved needles.

Injections at a Point Above the Superior Mesenteric Artery: Injections of 15 cc. were given forcibly through a straight No. 18 needle at a point several centimeters above

§ Definition of degree of injury is given under section "Injury of the Spinal Cord."

TABLE 2.—*Summary of Effects Produced by Intra-Aortic Injections of Fifteen or Twenty Cubic Centimeters of Seventy Per Cent Sodium Acetrizoate Below Renal Arteries Using Straight or Curved Needles*

Dog No.	Length of Study	Spinal Convulsion	Postinjection Status	Spinal Cord Injury	
				Lesion	Grade
15 cc. sodium acetrizoate, straight needle					
24	5 hr.	Severe	Paraplegia	General edema, cytolysis	++++
22	6 hr.	Severe	Paraplegia	Focal edema, cytolysis	++
23	8 hr.	Severe	Paraplegia	Scattered petechia	+
27	10 hr.	Severe	Paraplegia	Hemorrhagic necrosis	++++
18	14 days	Severe	Paraplegia	Myelomalacia	++++
20 cc. sodium acetrizoate, straight needle					
12	10 days	Severe	Paraparesis	Focal destruction	++
20	10 days	Severe	Paraplegia	Myelomalacia	++++
11	13 days	Severe	Paraplegia	Myelomalacia	+++
15 cc. sodium acetrizoate, curved needle					
35	4 days	Severe	Paraplegia	Hemorrhagic necrosis	++++
34	6 days	Severe	Paraplegia	Myelomalacia	++++
49	10 days	Severe	Paraplegia	Myelomalacia	++++
21	15 days	Severe	Paraparesis	Myelomalacia	+++

the superior mesenteric artery exposed through a high midline abdominal incision in nine dogs (Table 3). Spastic paraplegia occurred in only two. Spastic paraparesis occurred in both legs of one dog and in one leg only in three. The remaining three animals appeared normal. Examination of the spinal cords revealed severe necrosis in one, moderately severe necrosis in another, moderate necrosis in five, and no abnormality in two. Of the seven spinal cords exhibiting injury the segment involved was lower thoracic in three, lower thoracic and upper lumbar in two, lumbar in one, and lumbosacral in the other.

Injections into the Midthoracic Aorta: Injections of 15 cc. were given forcibly through a straight No. 18 needle at the midpoint of the thoracic aorta, exposed through a left thoracotomy incision, in four dogs (Table 4). Only one animal developed spastic paraplegia, one developed slight spastic paraparesis in one leg, and two were apparently normal. Examinations of the spinal cords revealed moderately severe necrosis in one, moderate necrosis in another, and minimal necrosis in two. The segment involved was thoracic (T-3 to T-12) in one, low thoracic in one, and lumbar in the two which had minimal injury.

Effect of Injection of a Smaller Volume.—Injections of Seven Cubic Centimeters Below Renal Arteries and Above Superior Mesenteric: The amount of 70% sodium acetrizoate

TABLE 3.—*Summary of Effects Produced by Intra-Aortic Injections of Fifteen Cubic Centimeters of Seventy Per Cent Sodium Acetrizoate Above the Superior Mesenteric Artery*

Dog No.	Length of Study, Days	Spinal Convulsion	Postinjection Status	Spinal Cord Injury	
				Lesion	Grade
26	7	Mild	Paraparesis	Focal destruction	++
31	7	Mild	Normal	Focal destruction	++
32	7	Severe	Paraplegia	Myelomalacia	++++
30	12	Severe	Paraplegia	Myelomalacia	+++
41	13	Mild	Paraparesis	Myelomalacia	++
52	13	Mild	Paraparesis	Focal destruction	++
42	16	Severe	Paraparesis	Focal destruction	++
43	16	Mild	Normal	None	.....
29	27	None	Normal	None	.....

TABLE 4.—*Summary of Effects Produced by Intra-Aortic Injections of Fifteen Cubic Centimeters of Seventy Per Cent Sodium Acetrizoate at a Middle Thoracic Level*

Dog No.	Length of Study, Days	Spinal Convulsion	Postinjection Status	Spinal Cord Injury	
				Lesion	Grade
56	5	Mild	Paraparesis	Focal destruction	+
53	6	None	Normal	Focal destruction	++
54	6	Mild	Paraplegia	Focal destruction	+++
55	6	None	Normal	Focal destruction	+

injected was reduced to 7 cc. for eight dogs. Injections were given at a level just below the renal arteries in four and just above the superior mesenteric artery in four (Table 5). As with other experiments a No. 18 straight needle was employed. Two of the four dogs injected below the renal arteries developed typical marked spastic paraplegia, one developed slight spastic paraplegia, and one was normal. The cord destruction was in the lumbosacral and coccygeal regions. Two of the dogs injected above the superior mesenteric artery developed spastic paraplegia; two were normal. Of the two which had cord injury the level was lower thoracic in one and lumbosacral in another.

Injury of the Spinal Cord.—Histopathological studies of spinal cords removed at autopsy several hours to 34 days after the injection of contrast medium, made by one of us (G. M.), will be reported in detail.[7] The injury focused upon gray matter, often completely destroying it over extensive stretches of the spinal cord with less serious changes in white matter (Fig. 2). The early phases of development of the lesions were observed in five animals killed within 48 hours of the injection. In three parenchymal edema of the gray matter and hydropic degeneration and chromatolysis of neurones were predominant. In another, petrechial hemorrhages, and in the fifth, heavy infiltration by hemorrhage in the gray matter dominated.

The later stages of injury were observed in 23 specimens removed from animals 4 to 34 days following the injections. There was absence of anatomical change in only four animals. For all dogs with anatomical changes there were clearly defined categories of progressive severity of injury. An arbitrary classification system, + to ++++, was developed and used in Tables 1 to 5:

+, Sparsely scattered microscopic foci of destruction of gray matter, present in one or more sections of spinal cord.

++, Multiple small (1 to 2 mm.) scattered foci of destruction of gray matter, with or without involvement of white matter or spinal nerves, distributed over 3 to 5 cm. of spinal cord.

+++, Massive focal destruction of gray matter, with or without involvement of white matter or spinal nerves, extending over 5 to 10 cm. of spinal cord.

TABLE 5.—*Summary of Effects Produced by Intra-Aortic Injections of Seven Cubic Centimeters of Seventy Per Cent Sodium Acetrizoate Below Renal Arteries and Above the Superior Mesenteric Arteries*

Dog No.	Length of Study, Days	Spinal Convulsion	Postinjection Status	Spinal Cord Injury	
				Lesion	Grade
Injection below renal arteries					
36	2	Mild	Paraplegia	General edema, cytolysis	++++
37	6	Mild	Paraplegia	Myelomalacia	+++
16	12	None	Paraplegia	Focal destruction	++
14	13	None	Normal	None	.....
Injection above superior mesenteric artery					
45	10	None	Normal	None	.....
46	10	Severe	Paraplegia	Myelomalacia	+++
47	12	Mild	Paraplegia	Myelomalacia	++++
44	16	Mild	Normal	None	.....

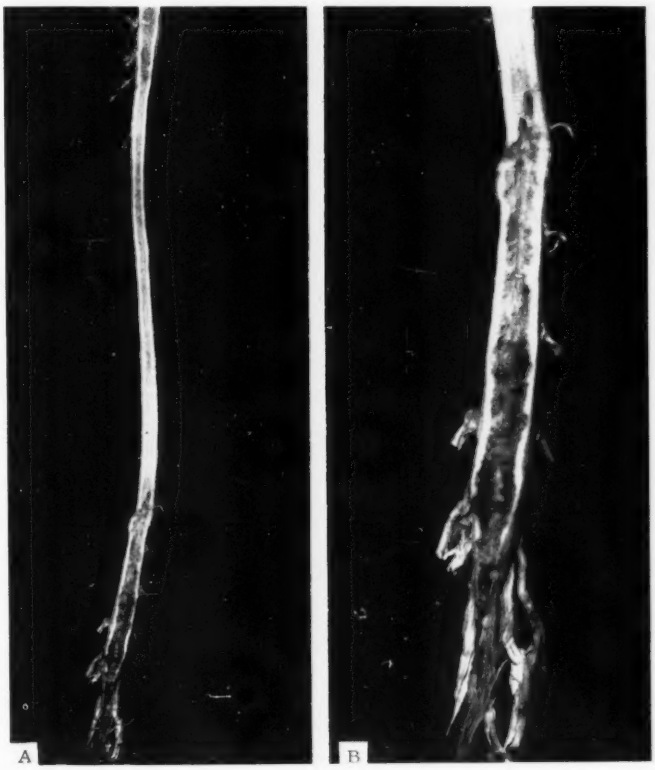

Fig. 2.—The longitudinal section of the spinal cord (*A*) and the enlargement of the lumbosacral region (*B*) evidence the segment of injury in a dog paraplegic for 10 days following the intra-aortic injection of 15 cc. of sodium acetrizoate.

++++, Complete or nearly complete destruction of gray matter, with or without involvement of white matter or spinal nerves, extending over 10 cm. or more of the spinal cord.

The necrotizing reaction was not confined to neurones but involved all fixed tissue elements with the exception of microglia. These latter cells played an active scavenger role, appearing as foamy macrophages in heavy numbers in the injured tissue as early as four days. In some lesions hemorrhage, angionecrosis, and thrombosis were prominent features during the first week of the reaction. The vessels involved in this destructive reaction were confined to the central gray matter. The vessels primarily involved were the branches of the anterior spinal artery. The lesions of severe degree began to assume a cystic character during the second week, and eventually the entire zone of liquefactive necrosis was replaced by a cavity. The borders of the lesions were often sharply defined, with a group of normal neurones located immediately adjacent to a zone of destruction.

All orders of size of such lesions were found, from microscopic foci to broad sweeps of necrosis extending throughout the gray matter. In the lumbar, and especially the sacral, cord the reaction often extended far into the white matter, so that the process approached a transection in extent. A common observation was the presence of scattered foci of degenerating fibers, particularly in the lamina propria. Incomplete degeneration of some of the lower nerve roots was also demonstrated accompanying the reaction of greatest severity.

Anatomy of the Spinal Circulation.—The arterial spinal circulation of 14 of the dogs was demonstrated by examination under a dissecting microscope and copied or mapped

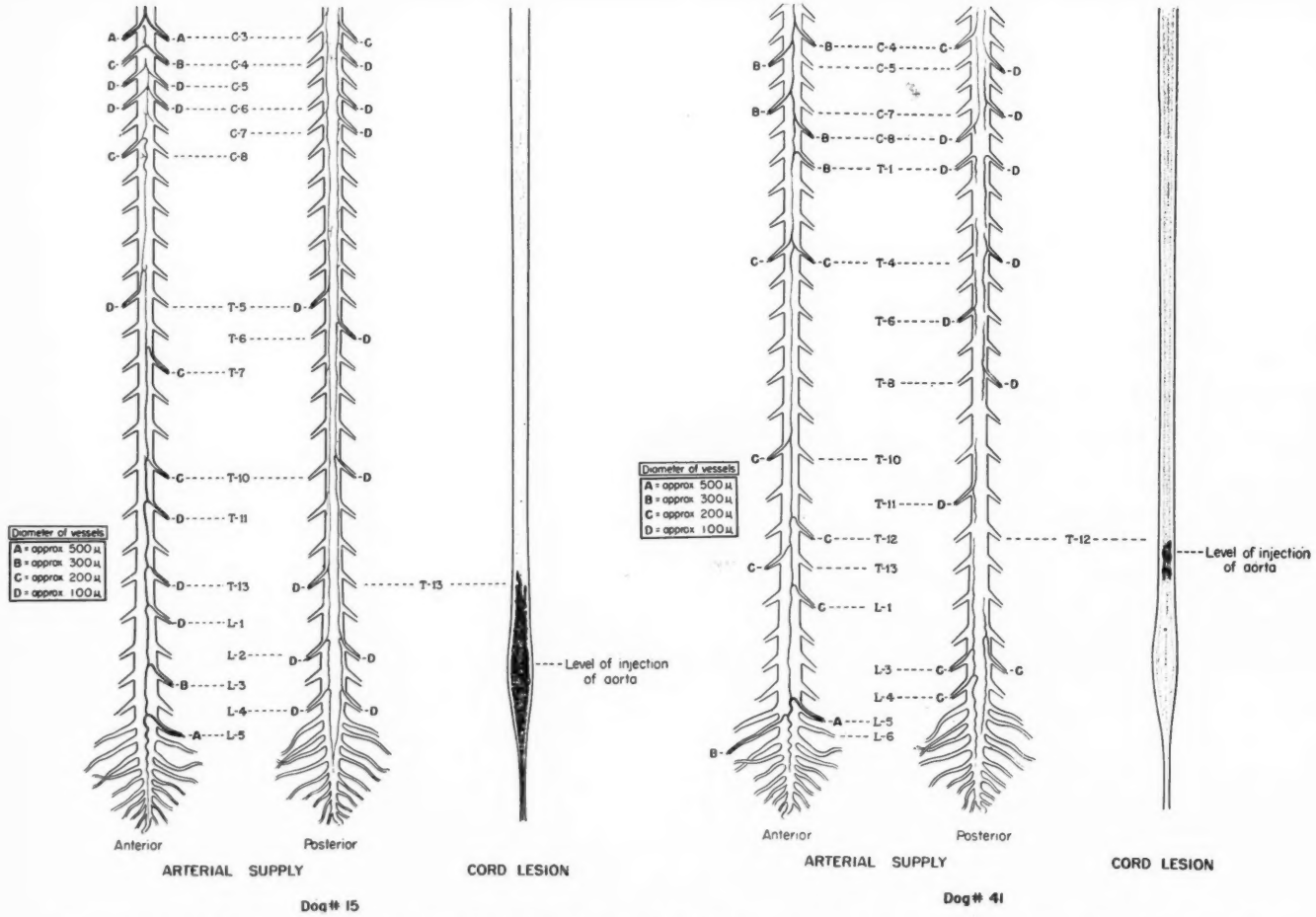

Fig. 3.—Drawings of the anterior and posterior surfaces of the spinal cords of two representative dogs, showing the arterial supply, the level of injection into the aorta, and the segment of injury. The largest radicular arteries enter at L-5.

individually with details of the distribution and the diameter of vessels. The radicular arteries were divided arbitrarily into four groups according to their approximate caliber in the postmortem state. Representative patterns of two dogs are shown in Figure 3 and are related to the level of the injection into the aorta and the segment of injury of the spinal cord. The diameter of the radicular arteries is identified by letters, *A* representing approximately 500, *B* 300, *C* 200, and *D* 100 μ. In general, the larger radicular arteries and the more continuous longitudinal spinal artery were on the anterior surface, the smaller and more irregular arteries on the posterior surface. The largest anterior radicular artery usually enters at the level of the fourth or fifth lumbar segment in the dog.

From 7 to 13 anterior radicular arteries and from 6 to 11 posterior radicular arteries supplied the spinal cords of the 14 dogs. The major blood supply to the lower regions of the spinal cord entered at L-4 or L-5. The major supply to the upper cord entered in the cervical region. The midthoracic segment of the cord had the poorest local segmental circulation. The anterior spinal artery ran along the anterior sulcus and was usually continuous. Branches of the posterior radicular arteries extended upward or downward along the posteriolateral sulci and tended to form two small and interrupted longitudinal arterial pathways. Since the spinal cords were removed before they were studied, it was not possible to determine the exact point of origin of each radicular artery from the dorsal segmental branches of the aorta.

Fig. 3.—Drawings of the anterior and posterior surfaces of the spinal cords of two representative dogs, showing the arterial supply, the level of injection into the aorta, and the segment of injury. The largest radicular arteries enter at L-5.

COMMENT

The spinal cord of the supine dog is readily susceptible to injury by contrast media containing iodine. It differs from that of man in that the canine cord extends to the seventh lumbar vertebra, whereas the human cord ends at the first lumbar. The level of the segment of injury of the spinal cord in the dog was usually higher than the level of injection into the aorta. Roentgenograms made as the injections were completed indicated that the radiopaque material which was forcibly injected cephalad rose several centimeters above the point of injection and against the blood flow within the lumen of the aorta. The observation that injections made above the superior mesenteric artery or in the midthoracic aorta caused less injury than those made just below the renal arteries may relate to the diversion of part of the contrast material into the renal and mesenteric arteries. The injections below the renal arteries sent a less diluted mixture through the blood stream toward the orifice of the largest radicular artery at L-4 or L-5. These observations suggest that aortography in man through a puncture site 2 or 3 cm. above the superior mesenteric and renal arteries would be associated with better dilution than injections made near their origin or lower. In some clinical problems injections can be made into the terminal aorta below the renal arteries, since in man the spinal cord terminates at L-1 and L-2.

A recent interesting study by Hol and Skjerven [8] has emphasized the role of position on spinal cord injuries in rabbits produced by injecting 70% iodopyracet. They usually gave two or three slow injections of 1.2 to 4 cc. volumes each. Their total injection time was 35 to 220 seconds. With use of this technique, lesions were produced with the rabbits in the supine position but not in the prone position. Our single rapid (5 to 10 seconds) injections which produced damage to the spinal cord in dogs were made with the animal in the supine position for those below the renal arteries and above the superior mesenteric, on the right side for those in the midthoracic aorta. Damage did not occur in six animals in the prone position. Clinically, most intra-aortic injections are given rapidly with patients in the prone position. Position, rate of injection, and rate of blood flow in the aorta are factors each of which should be considered in the clinical problem.

Studies of the spinal circulation in man have been reviewed and reported by Suh and Alexander.[9] According to their observations, six to eight anterior radicular arteries and five to eight posterior radicular arteries

supply the human cord. The anterior radicular arteries in man are larger than the posterior, and of these the largest, the arteria radicularis magna, usually enters along the second lumbar spinal root. This region should be avoided. The artery may enter at any segment between the eighth thoracic and the fourth lumbar.

Our series of patients from whom aortograms have been taken now numbers 43. Several sizes of needles have been employed, each larger than No. 18. Forceful manual injections of 50 cc. of 70% sodium acetrizoate have been made for the initial roentgenogram and repeated if the first roentgenogram was not satisfactory. The translumbar needle path has been directed well cephalad. The point of puncture in the aorta has usually been above the superior mesenteric artery, about 3 cm. above the renal arteries. No patient has exhibited any symptoms of injury of the spinal cord, but, as described in the introduction, one temporary and one lethal renal suppression have occurred. Smaller volumes of contrast media are now used.

The observation in dogs that 15 cc. of 70% iodopyracet injected below the renal arteries produced spinal cord injuries less frequently and of less severity than 15 cc. of 70% sodium acetrizoate, may in part relate to the higher iodine content of sodium acetrizoate, 32% greater. This higher iodine content accounts for improved detail of roentgenograms. It is interesting that only two of four dogs injected below the renal arteries with 7 cc. of 70% sodium acetrizoate developed marked spastic paraplegia, one developed only slight spasticity, and one had no lesion. Throughout these studies and at any of the three levels of injections, there was some variation from dog to dog, even though a standard technique had been employed. Studies of the arterial circulation were not made in all dogs. Therefore it has not been possible to correlate exactly the variations of injury with variations of blood supply. In patients variations of blood supply as well as of individual sensitivity or position during injection or level of injection have been suggested as responsible for cord injuries and should be considered in the clinical problem.

SUMMARY

Production of spinal cord injury has been accomplished in the dog by intra-aortic injection of radiopaque material. The lesions and the blood supply of the cord have been investigated. Large volume of contrast media, injection through a site near a major radicular artery, and use of a supine position have increased the frequency and extent of damage to the spinal cord.

DISCUSSION

Dr. E. A. Edwards, Boston: Suh and Alexander (*Arch. Neurol. & Psychiat.* **4**:659, 1939) emphasized that the cord is usually supplied by six to eight asymmetric branches of the spinal arteries. The largest branch (arteria radicularis magna) arises from a low thoracic or upper lumbar artery. A single segment artery is therefore of preponderant importance in supplying the cord. If a large quantity of concentrated medium happens to enter this artery, the cord is thus subjected to a powerful chemical effect.

Last month we observed a patient with a juxtarenal occlusion of the aorta who suffered paraplegia after aortography. Ten cubic centimeters of sodium acetrizoate had been used, and the left 11th intercostal artery had received much of the fluid. The patient had been very ill from hypertension and heart failure, and anoxia may have played a part in the complication. At autopsy softening of the cord was found. The 11th intercostal artery was not thrombosed, although such a process may possibly be responsible in similar cases.

Dr. Ralph A. Deterling Jr., New York: A few years ago we did some studies in the laboratory to evaluate the vasomotor responses of both dogs and human patients during the translumbar injection of contrast media. At that time we evaluated thorium dioxide (Thorotrast), sodium iodomethamate (Neo-Iopax), sodium iodide, and iodopyracet. At that time we did not yet have available a supply of sodium acetrizoate. It was quite interesting to observe very marked vasomotor changes peripherally with sodium iodide and less pronounced alterations with the organic iodides. At that time a review of the literature indicated that other investigators in the animal laboratory had used very large quantities of contrast medium, resulting in serious effects and even death in the animals. I mention this because in our own studies on dogs we used only 1 or 2 cc. amounts, these being more

comparable in regard to body weight with doses used in humans. I don't bring this up to criticize this paper, since it was pointed out that these studies were stress studies and that they did not deter the authors from using sodium acetrizoate clinically. In the past two weeks we had our first case of paraplegia in a human following the injection of a contrast medium, but I don't know enough of the details of the injection to do any more than record its appearance.

DR. GRIMSON, Durham, N. C.: The discussions by Dr. Edwards and Dr. Deterling are appreciated. In closing, I should like to emphasize again, as Dr. Deterling did, that we are describing an intentionally created cord injury caused by a large amount of contrast medium injected cephalad with a great deal of force. When the injections were made with the needle pointing caudad, there was less or no cord injury even with the same large amount of the contrast medium. All of us should be aware of the variations of blood supply to the cord that can occur from side to side or up and down. It seems wise to avoid aortic puncture near L-1 and L-2 in man, where the major radicular artery usually originates. The incidence of cord injury reported in patients is low enough that we should be cautious but should not abandon the present contrast media or the use of aortography. The renal as well as the cord injuries produced during aortography are low in incidence, but patients should be cautioned concerning the risk. We do not use aortography routinely; instead, it is used only when it is anticipated that the information gained will lead to a benefit to the patient which warrants a calculated risk procedure.

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Evaluation of Human Arteries After Long Storage in Nutrient Medium

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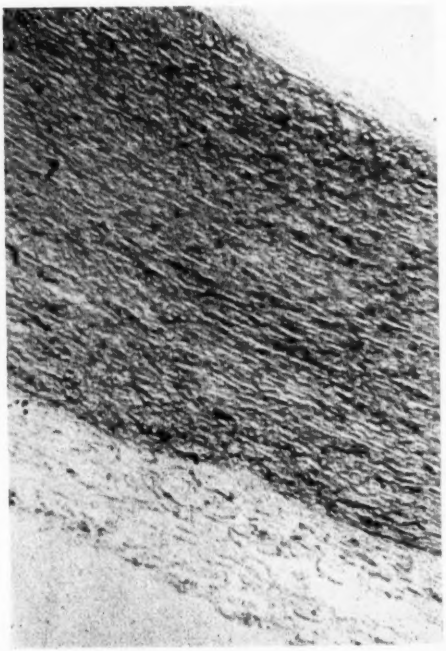
EDWARD B. C. KEEFER, M.D.
and
FRANK GLENN, M.D., New York

The successful transplantation of blood vessels in animals, reported by Carrel [2] and Klotz [10] (1910, 1925), along with the publications of Gross and co-workers * (1948) on the preservation and clinical utilization of homografts in man, has stimulated the present-day interest in human arterial implants. As a result, many investigators,† owing to the new techniques for the procurement and preservation of blood vessels, are evaluating the reactions which occur after implantation in the host. This is a natural result of the increasing demand for grafts to correct surgically the many congenital or acquired vascular abnormalities which only a short while ago were without treatment.

A sufficiently long period of time is necessary to evaluate experimental or clinical results. It seems therefore important to continue research on the fate of any type of transplant for long periods in an attempt to correlate functional results with histological findings. Since the experimental work of Swan and co-workers [19] with dog blood vessels, no further study has been made of the histological changes that occur after long storage in a "nutrient medium."

The New York Blood Vessel Bank [8] has maintained a supply of human blood vessels, preserved in various types of media, since July, 1949. With this material, an investigation was started in 1953 in order (1) to study the histological changes which occur in human blood vessels after long storage in nutrient media and (2) to compare these

Fig. 1.—Human aorta preserved in nutrient medium for 70 days. Weigert's stain; reduced from mag. × 100.



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* References 4 and 5.

† References 1, 3, 9, 12, and 14.

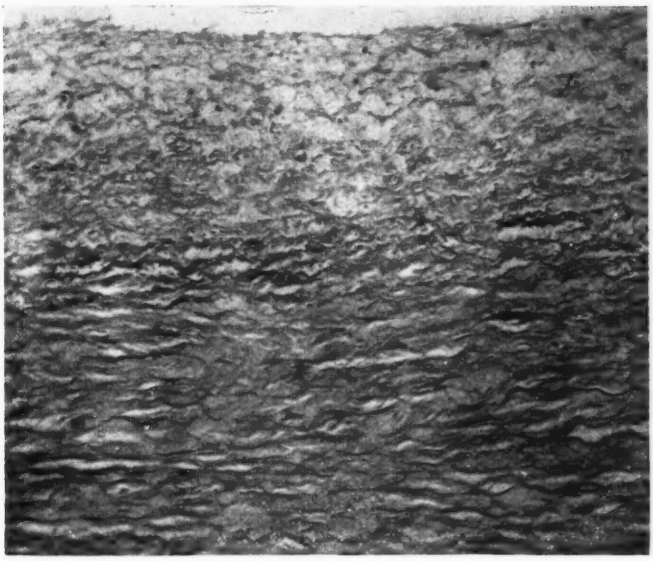


Fig. 2.—Human aorta preserved in nutrient medium for 189 days. Hematoxylin and eosin; reduced from mag. × 180.

changes with those taking place in transplanted blood vessels.

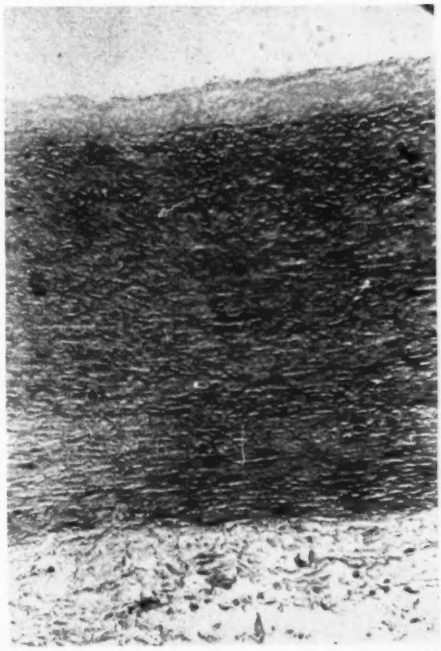
METHODS AND TECHNIQUES

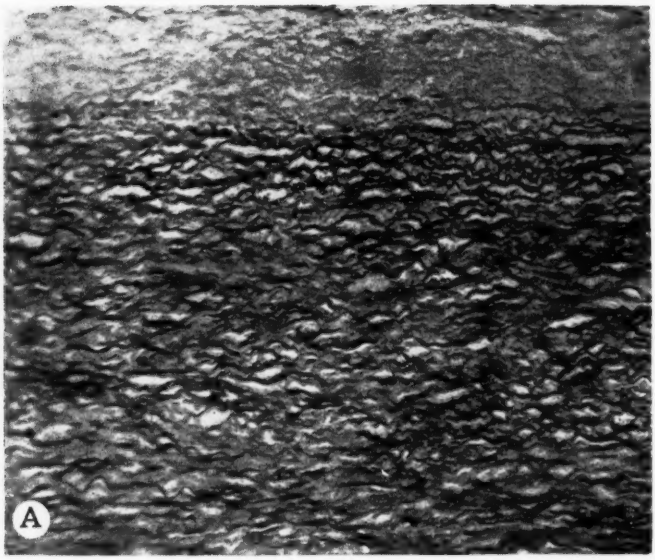
I. Procurement.—All vascular segments of this group were taken under sterile precautions from human donors. The donors' ages ranged from 17 to 37 years; 54% were male, and race distribution was 58% white and 42% Negro. Most of the donors were healthy persons who had died suddenly and were refrigerated immediately. Grafts were taken from 7 to 36 hours after death. A sample was taken for bacteriological studies immediately after procurement, and all contaminated grafts were discarded.

II. Preservation.—All grafts were preserved in a nutrient medium consisting of 85% buffered salt solution, 10% homolgous serum, and 5% antibiotics (penicillin and dihydrostreptomycin, 50 units/cc.) and kept at a constant temperature from 2 to 4 C. A sample of the nutrient medium was taken weekly for bacteriological studies. Sterility cultures for aerobes and anaerobes were observed for seven days, and any graft showing a positive bacteriological culture was immediately discarded.

III. Evaluation.—A critical evaluation of the pH of the storage solution was carried out by direct readings on a Beckman pH meter and by color observation of a known phenol red indicator in the medium. The pH was maintained between 7.2 and 7.6. Changes to pH below 7.2 were readjusted by addition of sterile $NaHCO_3$, and those above pH 7.6, by aseptically bubbling CO_2 through the

Fig. 3.—Human aorta preserved in nutrient medium for 301 days. Weigert's stain; reduced from mag. × 180.





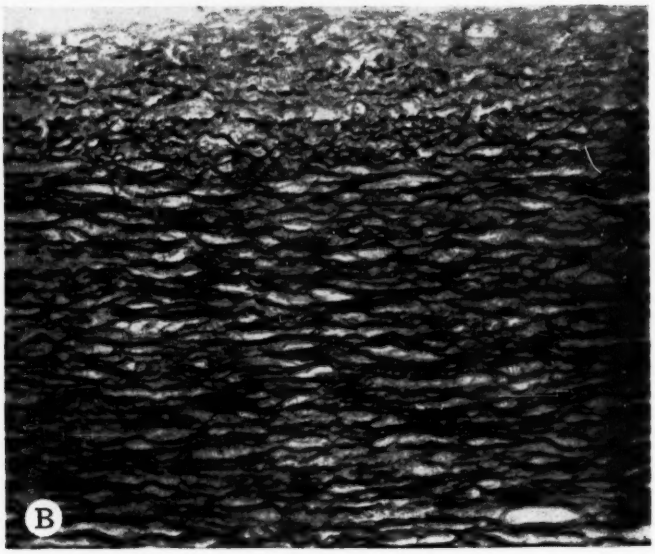


Fig. 4.—Human aorta preserved in nutrient medium for 366 days. *A*, hematoxylin and eosin; reduced from mag. × 180. *B*, Weigert's stain; reduced from mag. × 180.

solution. Changes to pH lower than 0.6 were considered an early indication of contamination, and extra bacteriological tests were made for those specimens. Otherwise, the medium was changed every 15 days.

IV. Histological Studies.—Three circular segments of the vessels were taken under sterile precautions every two weeks and fixed in 10% formaldehyde in Ringer's solution for 24 hours. Routine sections (5 μ thick) were made after the specimen was imbedded in paraffin and stained with Delafield's hematoxylin and eosin stain, Weigert's stain (resorcin-fuchsin) for elastic fibers, Masson's trichrome stain for smooth muscle cells and connective tissue, and Laidlaw's stain for reticulin fibers.

Fat studies were carried out on frozen preparations of Carbowax-imbedded sections, stained with Sudan black B.

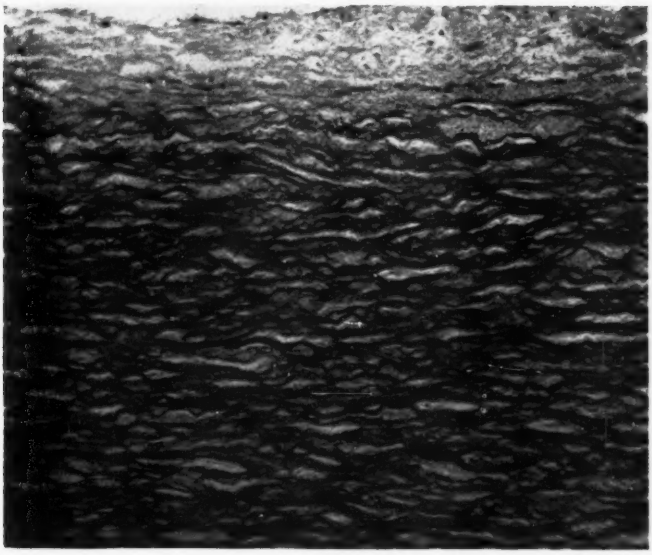


Fig. 5.—Human aorta preserved in nutrient medium for 433 days. Weigert's stain; reduced from mag. × 180.

Histochemical evaluations were done on these tissues by using toluidine blue stain for mucopolysaccharides and Schiff's reagent for aldehydes.

The tissue cultures of these specimens were carried out as follows: The adventitia was discarded in all instances to avoid false positive growth, and the vascular wall was isolated in squares of approximately 1 mm. and planted in Maximow slides, Carrel flasks (D3,5), or roller tubes (12 revolutions per hour).

A thin layer of one part chicken plasma and two parts Hank's solution covered the explants. When the plasma had clotted, in 30 to 45 minutes, two parts of homologous placental serum, three parts Hank's or Gey's solution, one part chick embryo extract, and one part ascitic fluid were added and the tubes were incubated at 37 C. The pH was adjusted from 7.4 to 7.8 with filtered CO_2, and the medium was renewed periodically (three to seven days). Daily observations were made under high and low magnification for a period of at least 45 days, and the growth rate was comparatively evaluated by mitotic index.

OBSERVATIONS AND RESULTS

The progressive changes that occurred from 70 to 639 days in human blood vessels preserved in "nutrient medium" at 2 to 4 C were in direct proportion to the length of storage. After a rapid modification of the cellular components during the first 120 days, there was a marked reduction in the speed of the degenerative process during the remaining period of observation.

Since the histological modifications of the three layers of aorta were different, we shall describe them individually.

1. *Intima.*—Modification of the endothelial cell configuration and nuclear pyknosis occurred in from 9 to 22 days.[16] After 22 days no cellular detail was recognizable (Figs. 1 to 5). The intima consisted of a thin acellular layer up to 526 days, which was well defined from the medium by selective elastic staining (Fig. 6).

2. *Media.*—There was a difference in the fate of the various components of this layer. The smooth muscle cells showed nuclear pyknosis and subsequent disappearance within the first 15 days. At the end of this time, hyalinization had taken place and occupied the space of the muscle cells, thus causing the media to become narrowed.

Extracellular structures remained longer than cellular tissue. Collagen fibers were still present after 188 days of preservation (Fig. 2). Elastic fibers were by far the most durable structures of the arterial wall and were definable until the maximum period of observation. As all the other elements of the

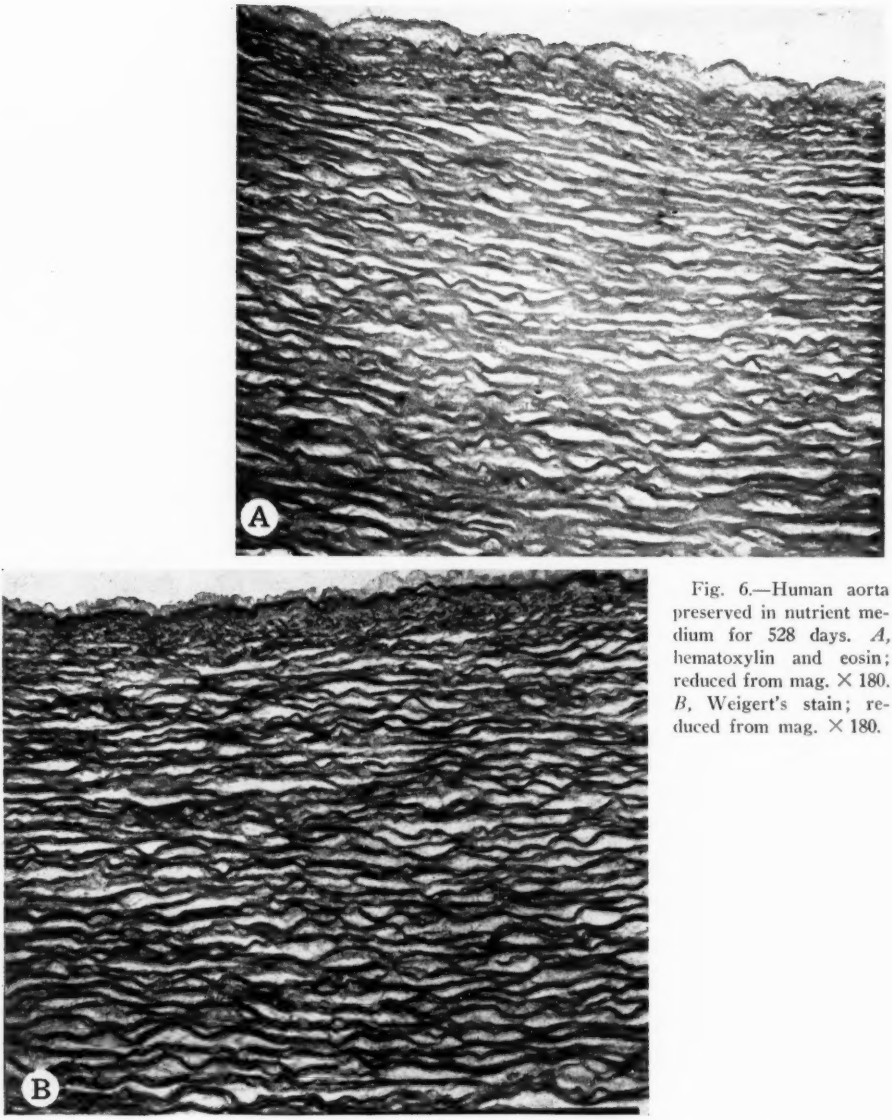


Fig. 6.—Human aorta preserved in nutrient medium for 528 days. *A*, hematoxylin and eosin; reduced from mag. × 180. *B*, Weigert's stain; reduced from mag. × 180.

arterial wall were modified, these fibers condensed, became thicker, and had an altered stain reaction (Figs. 7 and 9). For this reason, Weigert's stain was routinely used. After 500 days of preservation a constant separation of the elastic fibers was observed, due to the disappearance of the cellular elements (Figs. 8 and 10). The histological picture was similar to the one observed after four months or more of implantation in the experimental animal, as described by different observers.‡

The narrowed media was well defined and was separated from the intima by the internal elastic membrane up to 528 days (Fig.

‡ References 3, 7, 9, and 19.

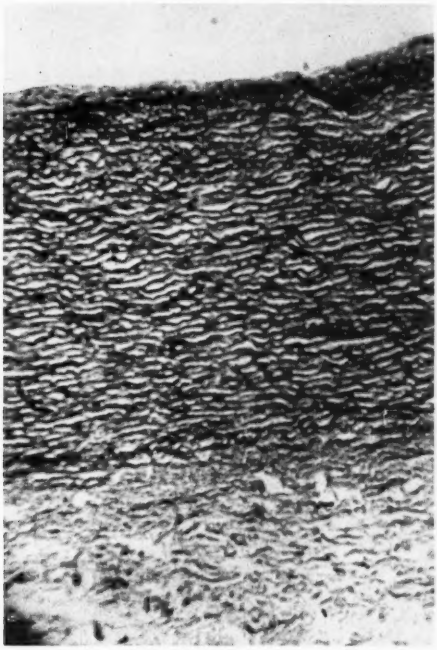


Fig. 7.—Human aorta preserved in nutrient medium for 560 days. Weigert's stain; reduced from mag. × 100.

6). Regardless of the storage time, fragmentation of the elastic fibers occurred in most of the cases in which contamination or extreme pH variations were not corrected. The histochemical studies for mucopolysaccharides and aldehydes were of no particular value.

3. *Adventitia.*—The connective structures were well preserved up to 301 days (Fig. 3). After this period of storage, fatty degeneration and nuclear pyknosis occurred and the adventitia was pale and undefined.

Tissue-Culture Studies

There was a close relationship between the postmortem period and the percentage of cell growth in tissue culture. In accordance with previous reports,§ these specimens have shown a marked degree of impairment in cell growth after 40 or more days of preservation in "nutrient medium." The cells varied in size and shape and were primarily fibroblasts. The nuclei were large and oval, and the cytoplasm was clear. Large fat granules were observed in some of the cells, as a possible degenerative process. At least six days were necessary to observe any growth in these cultures. It was impossible to define any endothelial cells.

COMMENT AND CONCLUSIONS

It has been well demonstrated that the transplanted vessel is only a framework for

§ References 3 and 11.

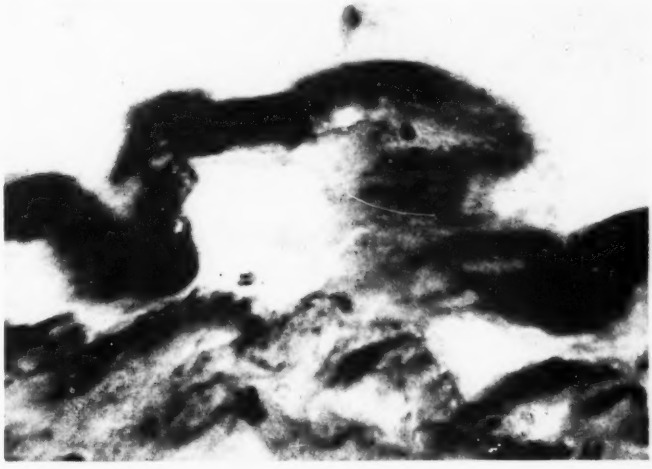
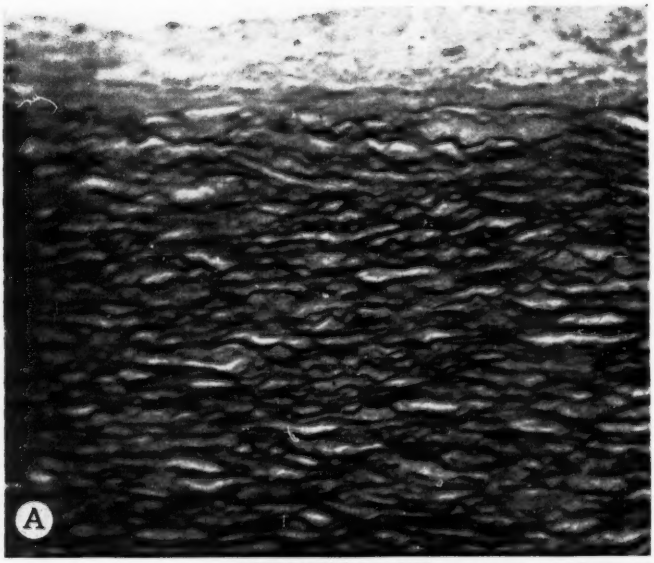


Fig. 8.—Histological detail of elastic fibers. Human aorta preserved in nutrient medium for 560 days. Weigert's stain; reduced from mag. × 900.



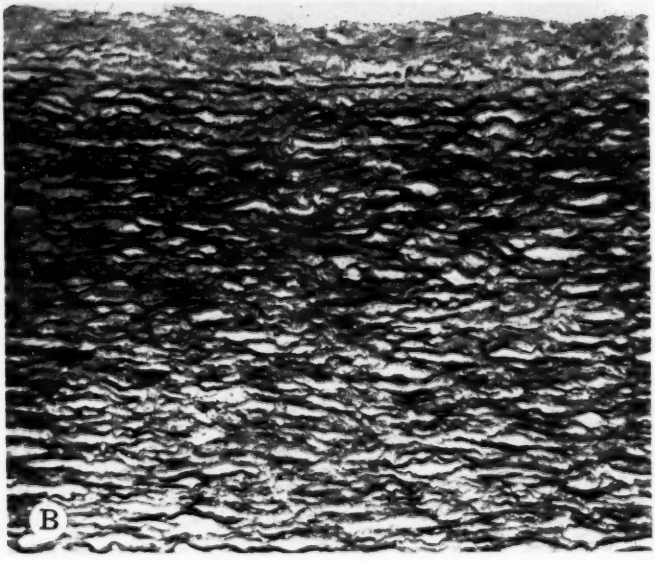


Fig. 9.—Human aorta preserved in nutrient medium for 639 days. *A*, hematoxylin and eosin; reduced from mag. × 180. *B*, Weigert's stain; reduced from mag. × 180.

the host cells. Most of the present methods for the preservation of blood vessels for experimental and clinical use do not pretend to maintain the viability of the cells. Sawyer and Pate [17] in their studies on the relationship of thrombosis and electric potentials of the arterial wall have pointed out that nonviable grafts are most likely to remain patent. According to a number of investigators,‖ the elastic fibers of the media are the most important structures for a successful functional result. The studies described in this paper do not advocate the utilization of vascular grafts preserved in "nutrient medium" for a long period of time. Other conditions,

‖ References 6, 12, 13, 15, 19, and 20.

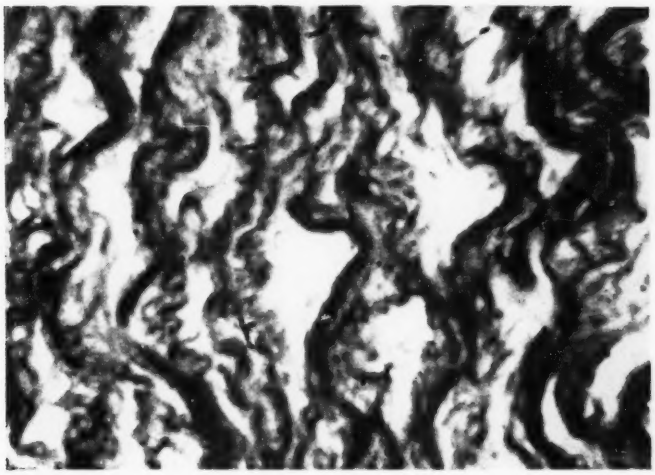


Fig. 10.—Histological detail of elastic fibers. Human aorta preserved in nutrient medium for 639 days. Weigert's stain; reduced from mag. × 500.

such as pH or contamination, as well as storage time, are significant factors in the preservation of elastic fibers. Histological controls by microscopic sections with specific elastic tissue stains are the best methods of evaluating the homograft.

SUMMARY

The progressive histological modifications in human arterial grafts after preservation in vitro up to 639 days in a sterile "nutrient medium" consisting of balance salt solution, homologous serum, and antibiotics in a controlled pH and temperature range of 2 to 4 C are described.

Although there is a rapid disappearance of cellular structures from the media of the vascular wall and growth of fibroblasts has not been obtained after 40 days of preservation, the elastic fibers remain without significant microscopic changes for long periods of time, providing that the pH is maintained within normal limits and contamination is avoided.

A similarity of the microscopic modifications of the preserved vascular graft to those of the implanted homograft in animals has been observed. Therefore, some of the changes which have been attributed to host reaction toward the grafted tissue may be explained as specific changes occurring in the nonviable graft per se.

In accordance with studies made in this bank and available literature on the fate of nonviable arterial homografts and heterografts preserved by different methods in vascular surgery, emphasis is made upon the importance of the normal characteristics of elastic fibers of the media for the successful use of these transplants.

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Bypass Arterial Graft Between Splenic and Iliofemoral Arteries

A Method of Treating Aortic or Iliac Obstruction with Unilateral Symptoms

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Occlusion of the abdominal aorta and iliac arteries can occur from thrombosis superimposed on arteriosclerosis obliterans, from thrombosis resulting from unsuccessful surgery on those vessels, or from embolism arising from intracardiac or other sources proximal to the area occluded. Restoration of continuity of the obstructed vessel by thrombendarterectomy * or by resection and graft † has been reported. The latter method has been the method of choice in our clinic.

There are certain patients, however, who are poor surgical risks or who present unfavorable local conditions for reconstruction of the vessels themselves, in whom a direct attack on the aorta or common iliac may seem inadvisable and a simpler, or bypass, procedure preferable. The use of the splenic artery as the vessel of origin for the bypass has been suggested by Glenn,[8] in a patient with low thoracic aortic coarctation, and by Freeman and Leeds,[9] in two patients with abdominal aortic occlusion. The technique presented here is closely related to theirs but entails the use of a homologous arterial graft from the end of the proximal segment of the divided splenic artery to the iliac or femoral artery below.

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From Veterans Administration Hospital and Massachusetts General Hospital, Chief, Surgical Service, Veterans Administration Hospital, and Associate Clinical Professor of Surgery, Harvard Medical School, Boston.

* References 1, 2, 3, and 4.

† References 5, 6, and 7.

REPORT OF CASES

CASE 1.—A 59-year-old man.

First Admission.—Sept. 9 to 16, 1953.

Chief Complaint: Backache and pain in the left leg for two months.

Present Illness: Two months before admission the patient suddenly awoke in the middle of the night with a cramp in the left leg, which soon disappeared. It returned, however, the next day and had persisted as an aching numbness. The diagnosis of sciatic rheumatism was made by his physician. The pain localized in the left buttock area. Nine days after onset he was treated by a chiropractor by means of manipulation, without improvement.

The patient had had angina pectoris of a mild nature for 20 years, relieved by glyceryl trinitrate (Nitroglycerin).

Physical Examination: There was muscle atrophy amounting to ½ in. loss of circumference of the left thigh and a ⅜ in. loss of the left calf, as compared with the right. The blood pressure was 170/88. No pulses or oscillations could be detected in either lower extremity.

Laboratory Data: Electrocardiogram showed a flattened T_1 with an inverted T_2 and T_3 interpreted as "possibly coronary thrombosis without myocardial infarct." The blood nonprotein nitrogen was 28 mg. per 100 cc.; the hemoglobin, 14.8 gm. per 100 cc., and the urine, negative.

X-Ray Examination: Chest x-ray showed the aorta to be somewhat elongated. The anteroposterior and lateral views of the lumbar spine showed lipping of the bodies of the vertebrae, with calcification in the abdominal aorta outlining a dilatation of 7×9 cm. The iliac arteries and the leg arteries were calcified. Barium enema was negative, and G. I. series showed a deformed duodenal bulb without an ulcer niche.

Fig. 1 (Case 1).—Preoperative aortogram.

Hospital Course: After the above studies had been made, the patient was discharged to make arrangements to return for operation.

Second Admission.—Oct. 19 to Nov. 2, 1953.

X-Rays: Aortogram and bilateral femoral arteriogram (by Dr. Robert Shaw) showed occlusion of the abdominal aorta extending up to, and partially occluding, the mouths of the renal vessels (Fig. 1). The femoral vessels were very irregular, with multiple partial blockades at various points.

Hospital Course: The cardiac consultant made a diagnosis of angina pectoris but believed that the patient "would stand any surgery which would be necessary." It was the opinion of the surgeon, however, that the patient was a greater than average risk for aortic resection.

Operation: Oct. 22, 1953, division of the splenic artery with placement of an arterial graft between it and the left external iliac artery; left lumbar sympathectomy.

Two incisions, one of about 4 in. situated in the left subcostal region and one of about 3 in. over the left inguinal ligament, were used. The graft was tunnelled from the divided stump of the splenic artery, underneath the transverse mesocolon, and retroperitoneally along the ureter until the left common iliac artery was encountered, when the

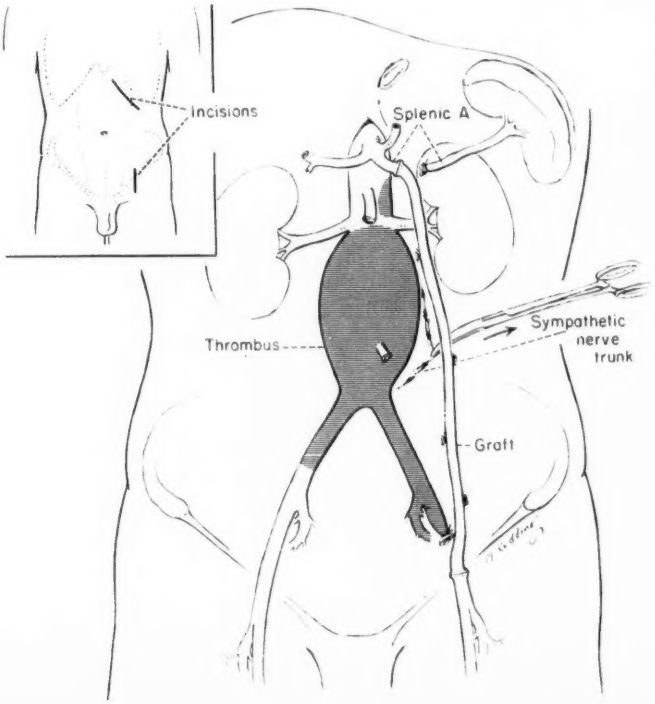

Fig. 2 (Case 1).—Diagram of operation performed.

Fig. 3 (Case 1).—Postoperative aortogram (eight days after operation).

course of that artery was followed. The external iliac artery was divided just above the inguinal ligament, the proximal cut end being ligated and the distal cut end sutured to the lower end of the graft (Fig. 2). A good flow was obtained through the graft. The femoral pulse and oscillations appeared immediately in the thigh. Two transfusions were given. Three hours after the operation a good left posterior tibial pulse was palpable, and two days later all pulses in the left lower extremity were present. The patient experienced immediate relief from the pain in his leg and was discharged eight days postoperatively. Aortogram before discharge showed the graft to be patent (Fig. 3).

Third Admission.—July 24 to July 25, 1954.

The patient entered a few hours after the sudden onset of severe pain and paralysis of both legs. Interval history showed that the rest pain in the leg had disappeared. The patient still had severe angina pectoris. He continued to have some intermittent claudication of the left leg. He had been seen five months after operation, at which time he had had a good left posterior tibial pulse and normal oscillations in the left calf.

Physical Examination: On the last admission there were no palpable pulses in the legs.

The patient died 36 hours later, and autopsy showed the graft to be open but there to have been extension of thrombosis up the aorta to involve the left renal artery. There was also infarction of the left colon. There was a pulmonary infarct and many scars of old myocardial infarcts.

Microscopic Examination: The junction of the graft with the host vessels at the splenic and at the iliac regions showed that there had been some old thrombosis across the suture line, which was fibrosed and covered with a smooth endothelial lining. Microscopically the union between the graft and the host vessel could be identified only by the fact that the hyalinized muscle tissue in the wall of the graft showed no nuclei, whereas that in the host did (Fig. 4).

Case 2.—A 62-year-old man.

First Admission.—Aug. 21, 1954; discharged Oct. 6, 1954.

Chief Complaint: Pain in the right leg.

Present Illness: The patient had had excision of an asymptomatic abdominal aortic aneurysm and aortic reconstruction by homograft at another hospital on June 11, 1954. He had entered there because of a duodenal ulcer which was visualized by x-ray and treated medically. Following operation the patient had severe pain in the right foot and leg and a few days after operation underwent incision and drainage and débridement of necrotic muscle in the calf of the right leg. Because of persistent pain in the right leg he was referred for consideration of further restoration of circulation.

Physical Examination: A healed abdominal incision; normal pulses in the left lower extremity; no pulses in the right lower extremity, with no oscillations and considerable ischemic rubor, and atrophy

Fig. 4 (Case 1).—Microscopic section of the union between the acellular graft, *A*, and the thickened external iliac artery, *B*, showing the superimposed layer of organized thrombus, *C*.

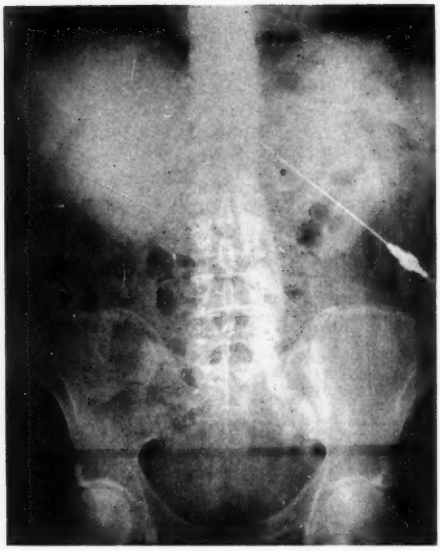

Fig. 5 (Case 2).—Preoperative aortogram.

of the right foot were found. There was a healed incision over the lateral aspect of the right calf. In addition to this the patient appeared jaundiced.

A diagnosis of homologous serum jaundice, presumably on the basis of transfusions at the first operation, was made. The patient was treated with rest, a high-calorie diet, and vitamin K. The jaundice gradually subsided.

Second Admission.—Nov. 15 to Dec. 20, 1954.

Interval History: The patient continued to have the same pain in his right leg. His weight and nutrition had improved.

Hospital Course: On Nov. 16, 1954, aortogram was made which showed obstruction of the right iliac artery from the bifurcation of the graft well down into the external iliac artery (Fig. 5).

Operation: Nov. 29, 1954, division of splenic artery with placement of an arterial homograft between it and the right common femoral artery. The graft, having been united to the stump of the splenic artery by end-to-end suture, was made to tunnel under the transverse mesocolon and to follow the course of the right ureter to the right iliac artery and thence down to the femoral artery, to which it was sutured end-to-side (Fig. 6). The areas rep-

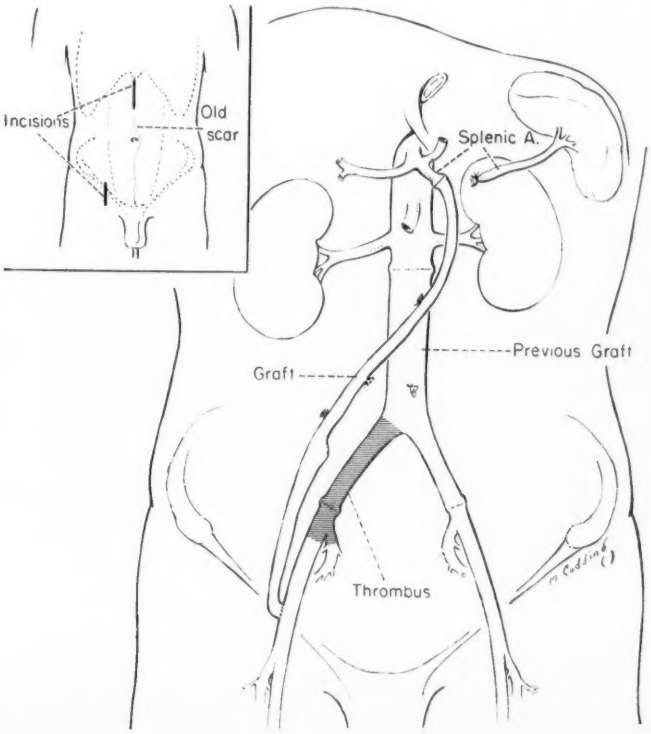

Fig. 6 (Case 2).—Diagram of operation performed.

resenting the old graft were not dissected. Incidental findings at the operation were an active duodenal ulcer and an abdominal aorta and left iliac artery which felt normal to palpation. Oscillations were present in the calf immediately after operation. Pulse returned to the foot within two hours after operation. The patient did well and had no further pain in his leg. Postoperative aortogram showed a patent graft (Fig. 7).

Third Admission.—March 29 to April 15, 1955.

The patient had been well since discharge until March 29, when he was admitted in shock. Diagnosis of rupture of the homograft was made, and laparotomy was performed. One thousand five hundred cubic centimeters of blood were found in the peritoneal cavity, and an area of possible leakage of the graft which had sealed over was found at its midportion just above the mesoileum and the ileocecal valve. There was an area of redness, thinness, and dilatation of the graft at this point, which had apparently been the place where the stump of the hypogastric artery of the graft had been sutured (the graft being an iliofemoral segment). A lateral excision of the ragged area was made, and the edges of the defect were sutured over and over. A patch of external oblique fascia was sutured over the area for reinforcement, and the abdomen was closed.

Postoperatively the patient did well, and aortography showed the graft to be patent with a possible small aneurysmic dilatation at the area of rupture

Fig. 7 (Case 2).—Postoperative aortogram (10 days after operation).

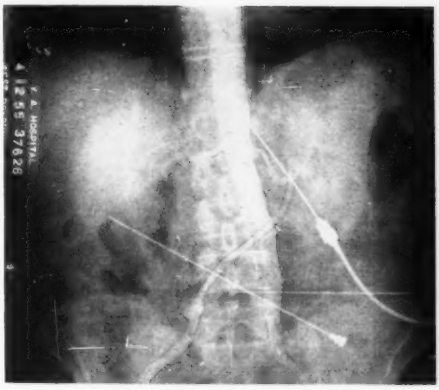

Fig. 8 (Case 2).—Aortogram four and one-half months after first operation, two weeks after second operation.

(Fig. 8). The patient has remained well during the brief period since leaving the hospital.*

COMMENT

In Case 1 the indication for the omission of a direct attack on the aorta was advanced cardiovascular disease. The patient's death seven months later from other complications of arteriosclerosis seemed to support the decision. The indication in the second patient was that of previous surgery on the aorta in the form of arterial graft replacement following resection for aneurysm. In the latter, dissection of the previous graft in order to accomplish an anastomosis to it might have been possible but in view of surrounding fibrosis seemed unwise. The above two indications appear to us to be the principal ones for the employment of the procedure. As experience with aortic resection increases it is possible that the first indication will be used less frequently, since, as is true in all such experience, operations become less "major" as time passes.

The technique employed appears simpler than the use of the splenic artery alone, as advocated by Freeman. Splenectomy was not necessary in either case, and the dissection of the splenic artery from the pancreas was avoided. Furthermore, it is doubtful that the splenic artery would have been long enough in either case to reach to the region of the

inguinal ligament, where these lower anastomoses were done. Even when the splenic artery is long enough to reach below the block, furthermore, the most favorable site for an end-to-side anastomosis of the lower end of the bypass may not be directly below the block but at a softer point in the artery more inferiorly.

The ability of the stump of the splenic artery and the graft to carry enough blood to support activity in a lower extremity seems established by these two cases. In Glenn's patient with coarctation the aortic flow was doubled by the use of the splenic artery (aortographic evidence), and the diastolic pressure in the arms, which had been previously elevated, was lowered almost to normal. One of Freeman's patients demonstrated pedal pulses in both limbs following splenoiliac anastomosis and ilioiliac anastomosis, and the patient could walk a mile before experiencing weakness. There was, however, some evidence of impairment of good pulsatile flow in that the oscillometric readings and the reactive hyperemia test were below normal when the splenic artery was thus used to supply normal blood flow to both limbs.

The episode of hemorrhage from the graft several months after operation in Case 2, with possible aneurysm formation, was disturbing. This event, however, cannot be taken as a condemnation of the concept of the operation but as some undiagnosed error in the preparation of the graft in this individual patient. This occurrence within the abdominal cavity is more hazardous than it would be, for example, in the thigh. It cannot be argued, however, that the type of graft described is more subject to such an untoward event than is an aortic bifurcation graft. It is of interest that in one of Freeman's patients where no graft was used there was a disruption of the splenoiliac anastomosis 11 months after its construction. Another criticism of the operation is that the splenic artery may be too small or too arteriosclerotic to use. I am not yet prepared to state now frequent this may be the case. A third patient has been operated upon with this procedure in mind, and a satisfactory anastomosis between the splenic artery and graft could not be made. Although the artery in this case was small, the problem of exposure and other technical considerations were, I believe, equally responsible for my inability to effect the anastomosis.

SUMMARY

A technique of bypassing an obstructed aorta or iliac artery by inserting a homologous arterial graft between the end of the proximal segment of the divided splenic artery and the iliac or femoral artery is presented.

Indications for the procedure are the following: (*a*) a patient with aortic or iliac thrombosis and ischemic pain in one lower extremity who is too poor a risk for a direct attack on the aorta or iliac artery and (*b*) a patient with similar thrombosis in whom an attack on the aorta or proximal iliacs is unwise because of the fibrosis resulting from a previous unsuccessful attempt at reconstruction.

Two illustrative cases are presented in one of which it was possible to examine the graft at autopsy seven months later. The symptoms of unilateral rest pain, which had been disabling in both patients, were completely relieved.

DISCUSSION

Dr. Elliott Hurwitt, New York: Dr. Ochsner, members, and guests, I rise to congratulate Dr. Warren on his ingenious use of the splenic artery in this situation and to focus attention on the availability of this wonderful splenic artery as a pinch hitter in various problems encountered in the body. A long length of splenic artery can be removed, cut up into pieces, and used as a fabricated graft of any diameter, anywhere in the body. The splenic artery can be used as a utility outfielder in such situations as used by Dr. Warren and by Dr. Freeman. It can also be used as a utility infielder, to replace compromised visceral arteries, and I should like just to call to your attention our first human splenorenal arterial anastomosis. Some time ago we reported a series of experiments in which the splenic artery was used to replace the renal artery, the hepatic artery, or the superior mesenteric artery in dogs.

[Slide] This is a man of 44 who came to the hospital in January with a typical Leriche syndrome

Aortogram by Dr. Haimovici showed a complete block of the aorta at this level. Resection was done by him at that time with replacement by a graft, and, because of severe obstructive arteriopathy of the iliac artery, obstruction of the graft took place. Aortogram was repeated in March and showed complete obstruction right to the level of the renal artery; because of the threat of this ascending thrombosis to involvement of the renal arteries, an end-to-end left splenorenal arterial anastomosis was performed, in March. One month later an intravenous pyelogram was repeated, showing good function in both kidneys.

DR. RICHARD WARREN, Boston: I should merely like to thank Dr. Hurwitt for his discussion.

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Two- to Four-Year Behavior of Vein Grafts in the Lower Extremities

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Arterial grafts are apparently now preferred by many to replace segments of peripheral arteries. However, vein grafts, either autogenous or homologous, are still the most available, and it is important to evaluate the long-term results. Various objections raised to the use of vein grafts are, namely, the dilatation under arterial pressure, the tendency of vein grafts to close, and technical difficulties in their placement. Actually, one must differentiate several aspects of the problem. First, vein grafts used to replace segments of arteries which have been injured and in which the vein graft is sutured to the normal artery proximally and distally usually stay open and function in almost every case. Here the flow of blood is good, and there is no obstruction proximally or distally. It is difficult, however, to find long-term follow-up of these cases. Secondly, vein grafts placed in a large artery, such as the aorta, without good support around them will dilate. This has been shown experimentally by a number of workers.* Support of the vein graft in the aorta by various means does reduce or even eliminate this dilatation. There is not much information as to what happens, insofar as dilatation is concerned, to vein grafts placed in the extremities of the human. This particular point will be elaborated on in the follow-up of the cases reported in this paper. Finally, the use of vein grafts in arteriosclerotic segmental obstruction constitutes an entirely different problem because of the inevitable partially diseased artery to which the graft is sutured proximally and distally in many cases.

Autogenous vein grafts have always been the graft of choice. However, it is our impression that the initial success of any graft is related to the flow of blood through the graft and to obstruction proximally or distally. Technical failures in placement of a vein graft in many cases are related to the small caliber of the vein graft, particularly when autogenous grafts are used. In recent years this has been overcome to a great degree by the dilatation of the graft before its placement by papaverine. It is certainly true that an arterial graft is easier to work with and suture in place than a venous vein graft.

The question of late closure or subsequent closure of vein grafts is a very important one and has previously been emphasized by Fontaine.§ Fontaine reported that in 25 cases of venous autografts 12 were patent one month after surgery and 5 were patent at the end of one year. He rightly emphasized the need for at least one year of follow-up in these cases. Malan [7] has also reported on subsequent failures in vein grafts in replacement of segmental occlusions.

Eastcott [8] has reported on his experience with arterial grafts in the femoral system.

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§ Fontaine, R., cited by Malan.[7]

Fig. 1.—Arteriogram of femoral autograft taken six months after operation.

He believes that vein grafts are unsatisfactory for replacement of segments of peripheral arteries in arteriosclerosis. An arterial graft was placed in the femoral artery in 13 patients, with four immediate failures, one resulting in amputation. Nine patients had good pulses immediately following surgery. Two later had thrombi, one necessitating amputation. In other words, 6 of the 13 patients had excellent results.

It is not the purpose of this paper to review again the indications for resection of segmental arteriosclerotic occlusions.† A review was made of the successful cases of replacement of segments of femoral artery by vein grafts which were reported two years ago.[11] At that time we reported 30 cases, with an initial failure rate of 50%. Of the 15 successful cases, 1 bilateral, all were followed for a period, therefore, of two to four years. The initial failure rate of 50% is higher than the recent reports, in which 80% to 90% immediate good results are reported. In a number of our earlier cases the failures were due to the use of anticoagulants. Also, some of the failures were due to the small caliber of the vein grafts, and in a few of the cases there was improper selection in that the patient actually had diffuse disease, with both proximal and distal obstruction being discovered at later dates. Of the 15 successful cases the patients were examined for peripheral pulses, and in most cases arteriograms were done from one to three times postoperatively to determine the patency and size of the graft. Seven of the fifteen patients have been followed more than three years, and eight, two years or more. On a follow-up examination 11 of the 15 cases showed pulses at the ankle, and in 8 of these 11 cases postoperative arteriograms were done, revealing patency of the grafts. Autografts were used in 11 cases and homografts in 4 cases. Homografts were obtained by vein stripping from another patient.

Two of the cases which have been followed for four years are of interest. The first case is that of a patient who previously had had a fracture of the femur, and a short segment of obstruction was removed adjacent to this fracture and replaced with a femoral autogenous graft. The large size of the graft is shown in the first postoperative arteriogram (Fig. 1). An arteriogram taken three and a half years postoperatively (Fig. 2) shows a small defect in its side-wall, presumably due to clot formation. In spite of

Fig. 2.—Arteriogram of the case shown in Figure 1 taken three and a half years after operation. Filling defect has appeared along lateral aspect.

† References 9 to 11.

the large size of the graft, it has remained open four years. This patient has remained free of claudication. The second case is that in which bilateral autogenous vein grafts from 25 to 30 cm. in length, respectively, were placed (Figs. 3 and 4). There has been no change in the caliber of these grafts, and the patient has maintained pulses at the ankle.

The question of whether vein grafts dilate in two to four years in the femoral system has been investigated. Small localized dilatations have been noticed in postoperative arteriograms, without general dilatation throughout the length of the vein graft. In one case in which a vein graft was used to replace a segment of artery removed during surgery for an arteriovenous fistula, it will be noted that the vein graft was too long and was kinked. In the two-year postoperative arteriogram a small aneurysmal dilatation was noted (Fig. 5). This case is not included in the 15 cases reported in this paper.

Figs. 3 and 4.—Bilateral saphenous autografts which have stayed patent for four years.

In the four cases in which the graft closed subsequently it is of interest to note that two of the four were homografts and two autografts. Of these four patients one was 59 years of age and the other three were over 60. The first case was that of a patient 66 years old in whom an autograft was used to replace a segment of femoral artery measuring 20 cm. Review of his arteriogram revealed that the patient had diffuse arterial disease with narrow arteries distally. This graft closed approximately six weeks after surgery. Failure to remove the entire diseased segment, regardless of whether it is closed completely, is an apparent cause of some late failures because of partial obstruction either proximally or distally. The second case in which the graft closed late was that of a saphenous homograft in a patient 62 years of age. This closure occurred approximately two months after surgery and was related to a severe cellulitis in this ex-

Fig. 5.—Arteriogram taken two years after resection of arteriovenous fistula and placement of vein graft. Note aneurysmal dilatation along medial aspect of graft.

Fig. 6.—Preoperative arteriogram. Obstructed segment only was removed, and subsequent closure occurred four months after surgery. Reexploration revealed recent thrombus in the graft.

tremity, together with a deep phlebitis. The resection was adequate in this case and on review should have succeeded and stayed open. The third case is that of a 59-year-old patient in whom a saphenous homograft was used. In this case a short segment was removed, measuring only 10 cm. in length (Fig. 6). The graft closed approximately four months after surgery. The closure had an acute onset, indicated symptomatically in the patient, and an arteriogram revealed a complete occlusion of a segment, similar to the picture prior to surgery. This patient was reexplored, and thrombosis of the graft of a recent nature was noted, together with

Fig. 7.—Postoperative arteriogram of a patient who subsequently developed closure of graft six months postoperatively. Resection of longer segment resulted in success..

a short segment of thrombosis into the proximal and distal artery. Here again it would seem that the resection was inadequate and was a possible cause of the late failure. The lumen of the graft was adequate and contained a recent clot. The fourth delayed closure occurred in a 60-year-old patient, and the loss of pulses occurred approximately six months after surgery. A saphenous autograft was used. The postoperative arteriogram is shown in Figure 7, and after closure another arteriogram showed the segment of occlusion. Reexploration of this case showed an inadequate resection and partial obstruction above, removal of which and replacement with a new graft resulted in success.

COMMENT

In our hands there has been a fairly high rate of initial failure with resection of segmental occlusions and replacement by vein grafts, namely, approximately 50%. Some of this failure has been due in early cases to large hematoma formation with the use of anticoagulants and also because an inadequate amount of diseased artery was removed. One is always faced with the fear of removing an important collateral. Furthermore, no doubt some cases of diffuse disease were included in which the disease process was so widespread that even with removal of the obstructed segment a graft would not stay open. Of the successful vein grafts which have been followed, it would appear from the postoperative arteriograms that there is some tendency to dilatation of weak spots in the wall of the vein graft and that no general dilatation throughout the length of the graft occurs, at least in the follow-up period in these cases. Subsequent closure of vein grafts following initial success has been observed in four cases previously elaborated upon, and it is noted that failure to remove an adequate segment together with improper selection of patients, that is, selection of a patient with marked diffuse disease, has been responsible for the late failures, rather than a fibrosis of the vein graft itself. This has been demonstrated in two cases which have been reexplored. Also, the late failures occurred in patients in the older age group, namely, 59 years of age and above.

SUMMARY

Fifteen patients who have had successful placement of vein grafts for a segmental arteriosclerotic occlusion have been followed two to four years.

Localized aneurysmal dilatations have been noted, but no general dilatation throughout the length of the graft has occurred in this period of follow-up.

Late closure of vein grafts, at least in the cases reviewed, seems to be related to improper selection of cases or inadequate resection of obstructed segments than to the fault of the vein graft itself.

DISCUSSION

DR. DENTON COOLEY, Houston, Texas: I have enjoyed Dr. Dye's interesting presentation. I believe we are all aware of the advantages of using autogenous grafts whenever possible. I should like to report our experience with arteriosclerotic occlusive disease of peripheral arteries, which has recently been analysed by Dr. Crawford. There were 63 extremities treated by replacement or bypass of the occluded segments with lyophilized arterial homografts. These are exclusive of approximately 90 cases of Leriche syndrome in which lyophilized homografts were used. Of the 63 cases 58 were successful and 5 were failures. The failures were probably due to poor selection, and I believe that was Dr. Dye's conclusion. In order to maintain patency of the graft, there must be a patent arterial system distally. The longest follow-up in our cases is 19 months. Thrombosis has occurred rarely, and there have been no graft failures after the patient has left the hospital. If autogenous veins can be used with as satisfactory results as homologous arteries, I am sure we will all turn to their use. The use of papaverine solution in preparing these grafts appears to be a useful technique.

DR. RALPH A. DETERLING JR., New York: I should like to ask just two questions of the authors. One, in their own experience, what was the success rate of vein grafts compared with arterial homografts? I ask this because of the greater number of failures with vein grafts at Massachusetts General Hospital, as reported in *Surgery* some time ago. Two, I should like to hear from the authors what was the fate of the extremities in which the graft failed? In our own experience the limb is usually not much worse off unless there is incipient gangrene at the time of grafting.

DR. WILLIAM S. DYE, Chicago: We do not have a comparable experience between vein grafts and arterial grafts. Unfortunately, we do not have the availability of femoral arterial grafts that many of you have, and we have been forced to use vein grafts for that reason. We have wanted to try the arterial grafts, and certainly recent reports would indicate the arterial grafts have an 80% to 90% success rate, which is above that in our experience with vein grafts.

In the failures, there have been 2 cases out of the 15 which failed initially and which resulted in amputation. I believe that Dr. Deterling is quite right that most of the time in the failures the thrombosis occurs in the length of the graft itself and, fortunately, the collaterals stay open above and below and the limb is not lost. One of these amputations was a sequel of a massive hematoma formation in the extremity accompanying anticoagulant therapy.

ADDENDUM

Since this report was submitted for publication, one femoral vein homograft replacement developed a localized aneurysm 4 cm. in diameter as well as general dilatation throughout the length of the graft. The degenerative changes present in the wall of the graft were marked.

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The Experimental Use of Steel Mesh Tubes for the Replacement of Arterial Segments

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A large share of current research in vascular surgery is devoted to the development and testing of various materials which may serve as prostheses for the major arteries. The difficulties of obtaining and preserving aortic homografts and the consequent desirability of suitable substitutes are widely recognized. There is general agreement on most of the characteristics which the ideal vascular prosthesis should possess. Among these are inertness, durability, and ease of handling and sterilization. It should be readily available and preferably inexpensive. The recent reports of Huĭnagel [1] and Schumaker and co-workers [2] indicate that plastic tubes presently offer the most promising results.

This study on a group of dogs reports the use of fine mesh stainless steel tubes as replacement grafts for segments of the abdominal aorta. Solid tubes of various metals [3] have been used as arterial substitutes for many years with little success. Steel mesh, however, is a porous material which might be expected to behave differently from solid-walled metal tubes. The in vivo inertness [4] and the relatively low blood-wettability [5] of Stainless Steel are known. Tubes constructed of Stainless Steel wire mesh have been employed experimentally as replacements for tracheal segments,[6] and this mesh has had limited clinical use in vascular surgery for the reinforcement of aortic aneurysms.* The wide range of usefulness of "steel cloth" in many fields of surgery has been discussed by Babcock.[9] Steel mesh is composed of monofilamentous strands of wire having very uniform arrangement. It was believed that these experiments with porous slightly flexible tubes of a durable, nonreactive, easily sterilized, and inexpensive material might offer an opportunity to study some aspects of the problem of graft healing.

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METHODS

The technique of constructing and implanting the grafts was as follows: a small rectangle of steel cloth was cut with scissors from a sheet of 200-mesh stainless steel. This was perforated around all four sides with a small sharp needle of the same size as the arterial suture needle. The perforations were close to the edge and about 1.5 to 2 mm. apart. The rectangle could then be rolled into a tube and held in shape by a continuous 00000 black arterial nonabsorbable surgical (silk) suture, thus forming a longitudinal seam. The suture needle passes through the puncture holes previously made in the steel mesh, and the suture was tied at either end. Construction was simple and required only a few minutes to fashion a tube, the diameter of which was determined by the width of the rectangle of steel mesh. Usually tubes of several sizes were made in advance of operation, although a few were fashioned after inspection of the artery to be grafted so that the diameter of the tube closely approximated that of the artery. The steel mesh was washed with a detergent used for surgical instruments and autoclaved before the tubes were constructed.

Through a midline abdominal incision, the dog's aorta was exposed and a segment was isolated between two small Atraumatic arterial clamps. After

* References 7 and 8.

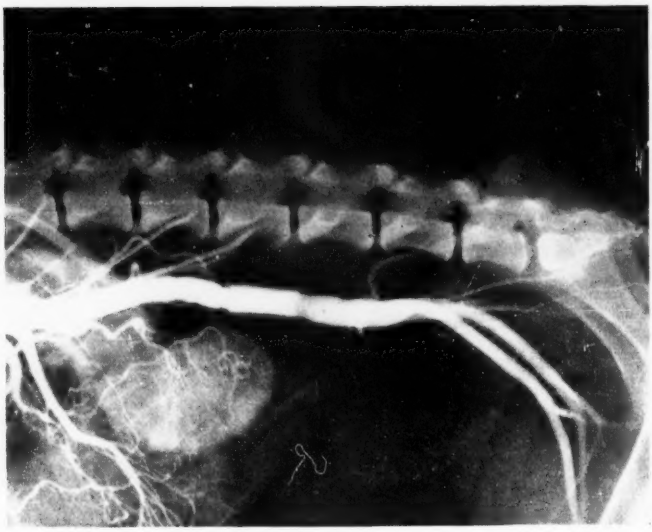


Fig. 1.—A patent steel mesh graft is in place a short distance proximal to the aortic trifurcation.

ligation of a few small branches, a portion of this segment was resected, this site being a short distance above the aortic trifurcation. The graft, which had been presoaked in the dog's blood for a few minutes, was then inserted. A 00000 arterial silk continuous suture was used for the anastomosis at each end, the needle passing through the puncture holes made in the graft. The distal occluding clamp was then loosened momentarily, allowing a retrograde flow of blood into the graft. Considerable leakage took place through the porous tube, although preclotting by soaking the tube in blood decreased this leakage. Several sponges were held about the graft to promote clotting in the interstices of the mesh while the distal clamp was momentarily released at brief intervals five or six more times. After about 10 minutes the graft was impervious to further bleeding and both clamps could be removed. Blood loss during clot-sealing of the mesh did not exceed 25 to 30 cc. The site of the graft was reperitonealized before closure of the abdomen. No antibiotics or anticoagulants were used.

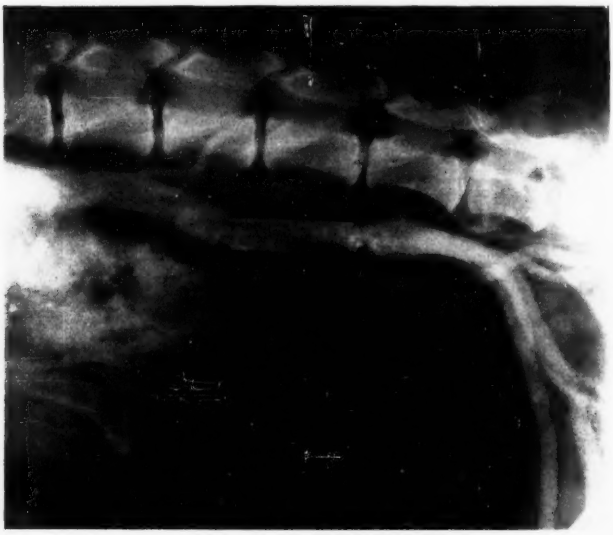


Fig. 2.—A patent steel mesh graft with some proximal angulation. Note slight aortic dilatation distal to the graft due to stenosis.

Fig. 3.—Although occluded, the metallic graft itself is visualized. The diverted stream of dye passes via large lumbar collaterals to fill the trifurcation area well.

RESULTS

Ten mongrel dogs were used, ranging in weight from 7.2 to 20 kg. Grafts were placed in the abdominal aorta and varied from 2.0 to 3.5 cm. in length and from 5 to 9.6 mm. in diameter. There were two early deaths on the first postoperative day, not due to graft failure. The remaining eight animals survived for study. The survivors had aortograms taken and were then killed when

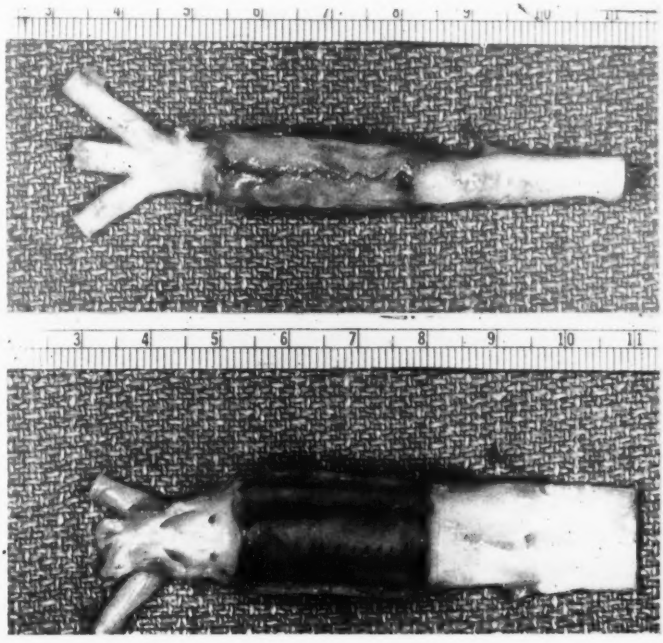


Fig. 4.—Above, an unopened graft is encased in dense connective tissue. The longitudinal suture line which formed the tube is seen. The graft is opened (below) to show the smooth new lining, which is darker owing to vascularity and underlying metal.

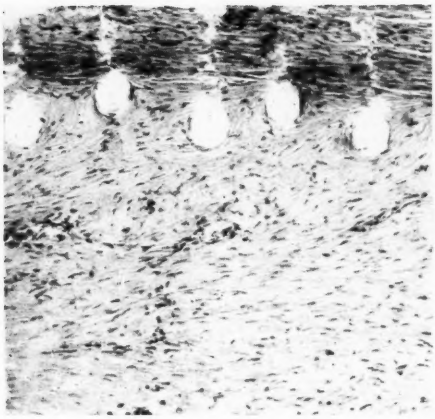


Fig. 5.—Photomicrograph of a longitudinal section through the wall of a graft. The holes were formerly occupied by circular strands of wire, which have been displaced into the lumen through the new intimal layer at the top; reduced from mag. × 100.

Fig. 6.—Photomicrograph of a graft wall under high power. The new internal lining (above) is composed of many layers of flattened cells which are in continuity with the investing connective tissue below. A fragment of metal remains in one of the wire holes; reduced from mag. × 250.

grafts had been in situ for 9 to 11 months. Specimens were removed at autopsy for photographs, measurement, and microscopic study. It was found that three grafts were occluded, two with dense, organized clots and one with a more recent red thrombus. Five grafts were patent, although one of these had a small mural thrombus at a point along the longitudinal suture line used in constructing the tube. The three occluded grafts were 5 to 6 mm. in diameter and were the smallest in the group. These dogs weighed less than 10 kg. The patent grafts ranged in age from 272 to 335 days.

Aortograms before death agreed with the autopsy findings, patent grafts being shown in Figures 1 and 2. In the cases of occluded grafts with old organized clots, good collateral supply to the distal aorta through the lumbar arteries was demonstrated, as seen

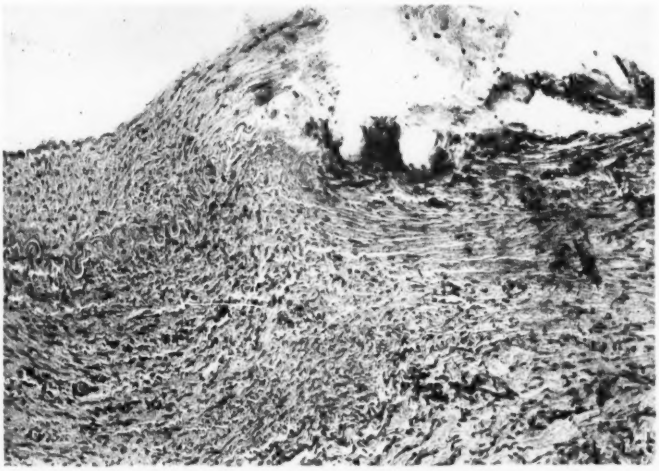


Fig. 7.—Aortic media and adventitia (left) blend into collagenous tissue surrounding a graft (right). Internal elastic membrane of the aorta is seen well. The junction of intimal layers has been disrupted by sectioning; reduced from mag. × 100.

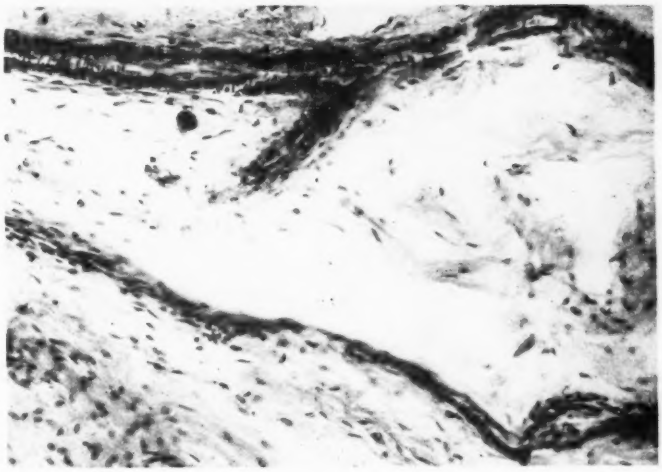
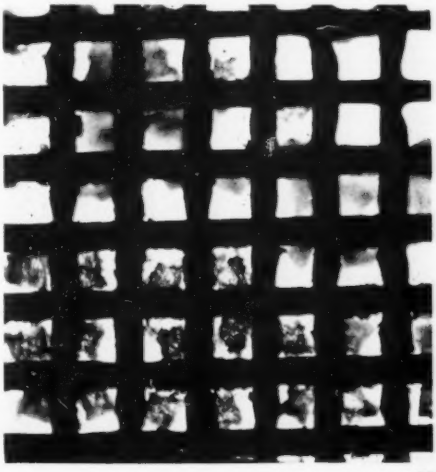


Fig. 8.—New blood vessels permeate the connective tissue surrounding a graft; reduced from mag × 200.

in Figure 3. All of the graft specimens were firmly embedded in rather dense scar tissue, so that their removal required sharp dissection. The entire area around each graft was more solid and inflexible than the original graft. Every patent graft was lined with a smooth, glistening inner layer (Fig. 4), which was pinkish-gray owing to the underlying metal. Microscopically there was no evidence of foreign-body reaction about any of the grafts. It was possible to cut sections through the wall of the graft by careful use of a hard steel microtome. One cut of the knife would displace the wire sufficiently so that the next several sections were free of metal. Figures 5 and 6 show sections in which the circumferential strands of steel have been displaced through the new internal layer of the graft, leaving holes which the wire occupied. At the junction of graft with aorta the media and adventitia of the artery blended into the fibrous tissue surrounding the graft, as may be noted in Figure 7. This fibrous outer layer of the graft was well supplied with small blood vessels (Fig. 8). Hematoxylin and eosin stains were used for routine sections. Connective tissue stains failed to reveal any elastic fibers in the tissues investing these grafts.

The histological picture of these grafts agreed well with the description of Voorhees, Jaretzki, and Blakemore[11] of relatively porous Vinyon "X" fabric grafts in dogs. The new inner layer is composed of multiple layers of small flattened connective tissue cells, which are continuous through the interstices of the steel mesh with dense connective tissue enclosing the grafts externally. Because a thin clot was formed between strands of the mesh in order to prevent leakage through these porous grafts, it is believed that the organization of this clot and formation of the inner lining of the grafts may

Fig. 9.—Magnified view of the steel mesh after removal from a graft. Bits of adherent tissue remain within the mesh; reduced from mag. × 80.



well be due to the ingrowth of fibroblasts through the mesh. A magnified view of the mesh after removal from a graft (Fig. 9) shows tissue clinging to the wire.

COMMENT

Several improvements in technique have been indicated by the late results obtained. One patent graft contained a small mural thrombus at a point of delayed break in the longitudinal suture line used in constructing the tubes. Less hazard of thrombosis would exist if this seam were closed with fine steel suture rather than silk. Further improvement would obtain by construction of internally smooth, virtually seamless tubes closed by electrical welding. Such tubes, of various diameters, could readily be cut to the desired length. The three grafts with smallest diameters (5-6 mm.) became occluded. Examination of these specimens suggested that thrombosis began at each end of the graft, where the artery was slightly narrowed and a suture line presented. Although the difficulty of maintaining patency of small grafts in the abdominal aorta of the dog is well known, elimination of the suture lines by use of an external ring of the Hufnagel type to afford multiple point fixation of the artery about these tubes would be advantageous. Initial blood loss when sealing the mesh against leakage, though not great, was nevertheless undesirable. This bleeding might be diminished by temporary application about the graft of thrombin-saturated sponges or absorbable gelatin sponge (Gelfoam) or by rapid coagulation within the interstices of the metallic graft by electrothermia, as was used in electrothermic wiring of aortic aneurysms.[10]

The results in this small series indicate that fine mesh Stainless Steel "cloth" may be used with reasonable success as an experimental type of porous slightly flexible arterial replacement. This material is not as easy to work with as fabrics, but because of its porosity it provides an opportunity to study the healing of arterial grafts in which the new internal and external layers communicate. There are many unanswered questions regarding the best arterial prosthesis, and among them are two fundamental issues yet to be decided. One is flexibility of the graft, and the other is its porosity. Certainly in areas where an artery crosses a flexion point, as in an extremity, a suitable graft must conform to the alterations in position. Here autogenous or homologous vein grafts have proved satisfactory. However, within the trunk the major vessels are subject to more limited change of shape. Even under these conditions inflexible grafts will reduce the lumen by kinking the artery at its attachment to the graft with slight changes in body position. Very flexible fabric grafts, if too loosely installed, may be prone to wrinkle, permitting thrombosis to occur. The ideal graft might be assumed to approximate the replaced artery in flexibility, even if inelastic. However, it appears that nearly all successful grafts become incorporated in fibrous tissue elaborated by the host, making them flexible only to the degree permitted by the investing scar tissue.

The porosity of a graft is another unsettled issue. If this is at all a desirable feature, the degree of porosity must be so limited that oozing through the graft material is not troublesome. Nonporous grafts offer no opportunity for the surrounding tissues to contribute to either the development or the maintenance of the layer which lines the graft. Whether a new intimal layer glides in from either end of a graft or originates chiefly from cellular elements of the blood stream, which in turn precipitate onto the early fibrinoid lining of a graft, is not a settled point. It does seem, however, that such a new internal layer, or "neointima," might be more rapidly and permanently formed if in contact with the tissues surrounding the graft. The patent grafts obtained in this study demonstrated that slightly flexible grafts were rendered more immobile by the walling-off effect of the tissue healing about them. It should be emphasized, however, that when grafting is done into human arteriosclerotic vessels the vessel of the host has lost most of its elasticity. The ideal graft from a hemodynamic standpoint would be

one whose physical properties closely resembled those of the vessel of the host. The excellent smooth lining of these experimental grafts may be due in part to the vascularization of the "neointima" by the surrounding tissues.

Since these experiments indicate that in the dog fine steel mesh is well tolerated, one might consider using this material in man to reinforce autogenous vein grafts. Actually, one of us (G. de T.) has placed steel mesh around abdominal aneurysms in three instances.[8] Two patients have been followed for two years, and the third patient, because of increasing pain and threatening perforation, has had the aneurysm resected by Dr. William S. Dye. The mesh was well incorporated into the wall and gave good support but did not surround the sac sufficiently to be of any protective value against rupture. An abdominal aorta or a common iliac artery which remains unusually weak after endarterectomy might be conveniently wrapped with steel mesh, but such a situation has not recently presented itself to us.

SUMMARY

Short tubes of 200-mesh stainless steel wire were used as replacement grafts for segments of the abdominal aorta in 10 dogs. Eight survivors were killed 9 to 11 months after grafting. Three grafts were occluded, as shown by aortography and confirmed at autopsy. Five grafts remained patent, although one contained a small mural thrombus. These patent grafts were lined with a smooth layer composed of multiple laminae of flattened connective tissue cells. The lining was continuous through the steel mesh with investing dense connective tissue. These outer tissues were well vascularized but devoid of elastic fibers. The presence of a robust "neointima" lining these grafts suggests that continuity of this layer with tissues surrounding the graft may be helpful and that a degree of porosity of arterial grafts is desirable. It was also observed that these slightly flexible steel mesh grafts became more rigid when incorporated in the scar tissue formed about them. The question of how much flexibility is desirable in major arterial grafts is again raised. The possible use of steel mesh for reinforcing vein grafts or thin arterial segments following endarterectomy is discussed.

Dr. T. E. Bolden assisted with the preparation of the microscopic sections, and Dr. C. L. Pirani studied the histological material.

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An Appraisal of Woven Synthetic Prostheses in the Vascular System

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Since the demonstration that a synthetic fabric could be used successfully for replacement of the aorta of dogs [1] there has been considerable interest in the clinical use of such materials. Unfortunately, because of the ready availability of these fabrics in textile stores, there has been much less caution exercised in the use of these materials than in the use of homografts. Many surgeons, often without adequate technical background or knowledge of the physical and chemical characteristics of the synthetic fabric, have proceeded to resect major arteries in patients and to implant synthetic prostheses. In a recent publication [2] we presented an analysis of the various synthetic materials currently available in fabric form. Whereas nylon, Vinyon-N, Dacron, and Orlon have all functioned well in the mammalian arterial system insofar as testing has been conducted, there have been certain reasons for favoring one material over another. This study also analyzed the specific physical characteristics of 16 fabrics suitable for blood-vessel replacement. Many of them were closely similar insofar as thread count, type of weave, thickness, denier of yarn, and porosity are considered. Although it would have been presumptive to recommend one cloth which all vascular surgeons should accept, the study did call attention to certain qualities which might be considered as desirable in a fabric designed for blood-vessel replacement. While our evaluation of synthetic fabrics is continuing, we selected two taffeta weaves of nylon yarn, one of moderate porosity and one of low porosity, as well as a taffeta of Dacron subjected to a moderate and a heavy calendering process, for evaluation in various sites in the vascular system. This report is concerned with the behavior of these fabric grafts in blood vessels of differing pressures as well as rate and volume of blood flow. The experimental data are not to be considered as final, since these prostheses have functioned for periods of time up to one year only. Nevertheless, these observations should have value if considered in proper perspective.

METHODS AND MATERIALS

Woven Materials.—Three fabrics of taffeta weave were selected for trial. In this construction each thread passes alternately over and under the adjacent one, in the warp as well as in the filler. Two of the fabrics were of 70 denier * multifilament nylon yarn of moderate twist. Nylon was chosen because of its great toughness and because of its satisfactory use in mammalian tissues since 1939. One fabric † had a rather low thread count, of 116×96 per inch, and a relatively high porosity,‡ of about 45. The other § had a count, of 166×116

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* Denier is the weight of 9000 meters of yarn as measured in grams.

† Supplied by Ethicon Suture Laboratories, New Brunswick, N. J.

‡ Porosity is determined by the number of cubic feet of air which pass through a square foot of fabric per minute at a pressure of 1.26 in. of water.

§ Supplied by Sol Lamport, 350 Broadway, New York.

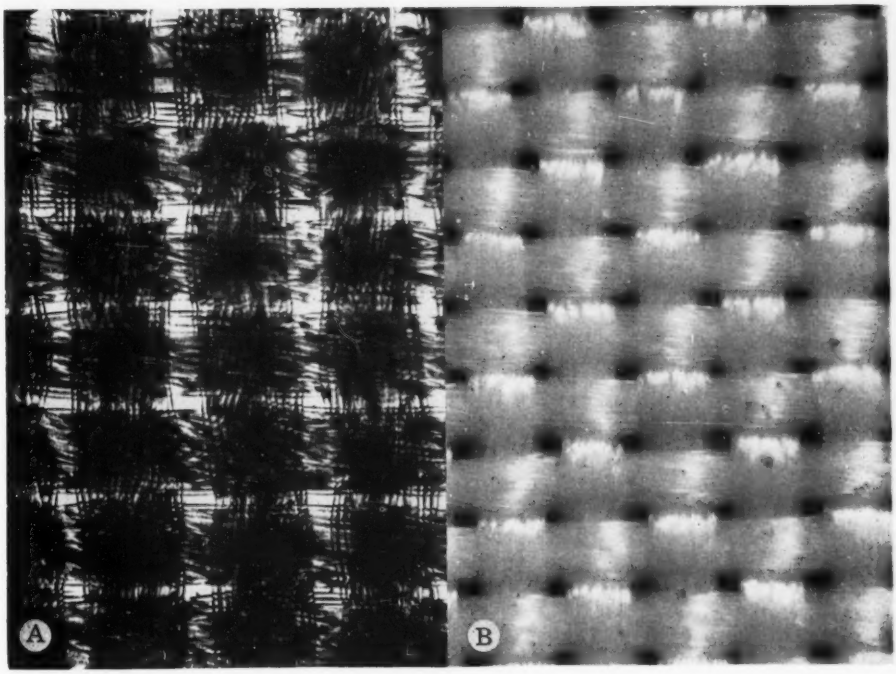


Fig. 1.—Photomicrographs of a nylon taffeta fabric of low porosity. *A*, transillumination. *B*, surface illumination.

per inch, and a porosity of only 16. The thickness of the finished fabric averaged 0.0045 in. The third fabric || was of Dacron with 40 and 70 denier multifilament yarn and a count of 116×100 per inch. The calendering ¶ process was used in the finishing process. In one type of fabric only a single side was treated. The porosity was therefore slightly greater in it than in the other, in which both sides had been calendered. The porosity averaged about 8 for the single-side and 4 for the double calendering, and the thickness averaged 0.00375 inch and 0.00275 inch, respectively. The lower porosity of the Dacron fabric as compared with the nylon one with similar thread count was the result of calendering. Heat and pressure flatten the yarn, thus reducing the size of the interspaces between threads and also producing a smooth surface (Figs. 1*A* and *B* and 2*A* and *B*).

Construction of the Fabric Grafts.—It is of importance to have exact measurements when preparing a prosthesis of synthetic fabric, in contrast to the approximate dimensions needed with tissue grafts. In consequence, we often have fabricated the replacement in clinical cases during operation, at which time exact dimensions could be determined. A caliper may be used for determining the diameter of the functioning vessel and the flat width calculated from the diameter by the formula $W=\pi D/2$.# A flexible metal centimeter rule is used to measure lengths, and a protractor is used to determine angles, as needed in bifurcation replacement. In diseased vessels the difference between outside and inside diameters may be appreciable, but occasionally preoperative visualization of the involved area may allow prediction of size. At times intimectomy performed at the cut ends of a diseased arterial segment will increase inside diameter to almost that of outside diameter. Angulation, buckling, or wrinkling of the fabric replacement may induce thrombotic occlusion, especially when the diameter is less than 10 mm.

In the construction of simple tubes of fabric, the cloth was folded and secured with pins. The exact measurements of the graft were drawn on the fabric with pencil. One centimeter of the fabric was turned back at the ends to produce a cuff after the proper length was determined. A lateral seam was then

|| Supplied by Sol Lamport, 350 Broadway, New York.

¶ Calendering is the process of passing fabric between heated rollers under pressure.

W=width; D=diameter; π=3.1412.

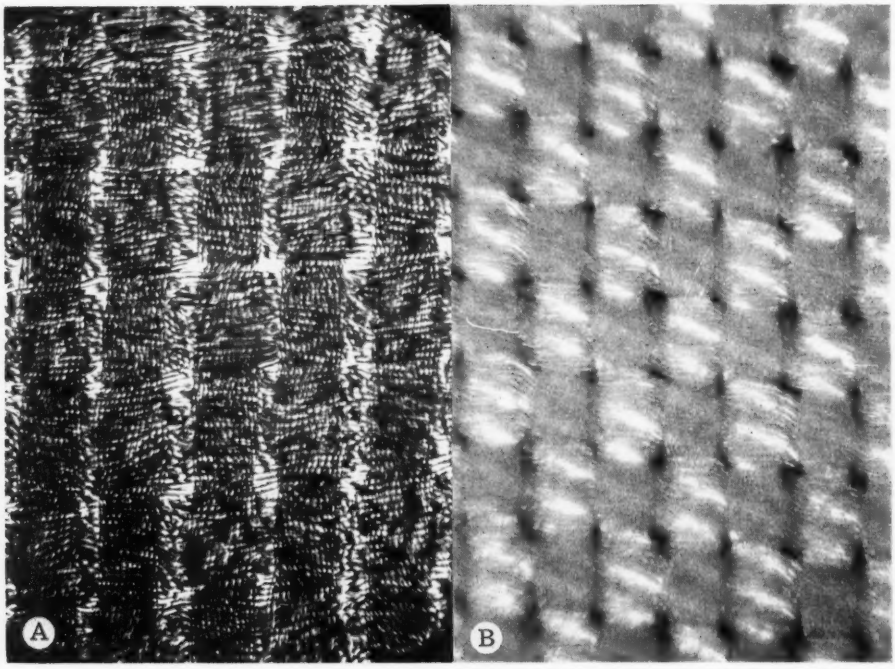


Fig. 2.—Photomicrographs of a Dacron taffeta fabric subjected to calendering to achieve low porosity. *A*, transillumination. *B*, surface illumination.

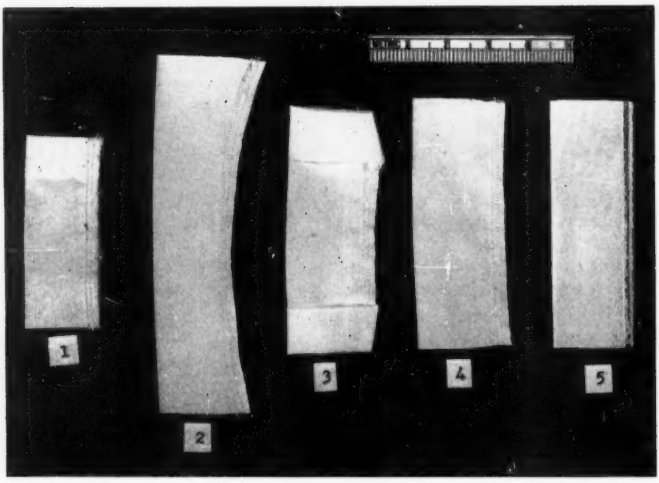
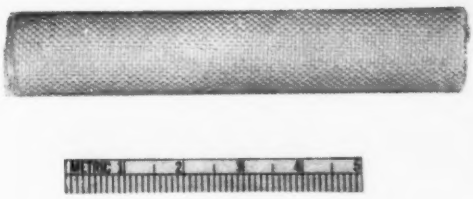


Fig. 3.—Preparation of tubular fabric grafts. (*1*) The cuffed ends are included in the double suture line of the lateral seam. (*2* and *3*) The ends are flared beyond the anticipated length of the graft. When the ends are turned back, cuffs are formed. The length of the graft can thus be varied. (*4*) Although the lateral seam has been made by a double line of sutures, the graft has been cut to length with a heated metal edge which fuses the threads. (*5*) The lateral seam has been made by heated bars which fuse the fabric. The ends have been cut with a heated wire.

sewn along the pencil line, to include the cuffs (Fig. 3). An additional reinforcing line was sewn about 2 mm. or so outside of the first row, employing the shortest stitch on a standard portable sewing machine. Nylon or Dacron twisted thread, size A, was used with a No. 9 needle. We have usually used the same material in both thread and fabric. One disadvantage of preparing the graft with this method has been that no satisfactory adjustments can be made in the length of the graft. The turning of an



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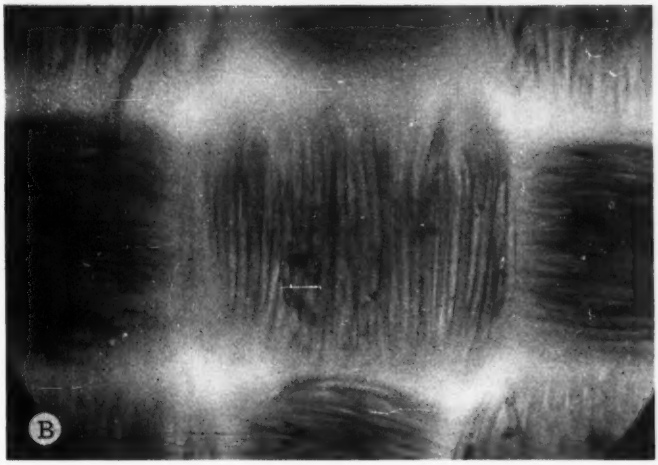


B

Fig. 4.—Woven seamless tube of nylon. *A*, external appearance. *B*, photomicrograph by transillumination, with same magnification as in Figures 1 and 2.

additional cuff, should the replacement be too long, reduces the effective lumen at the end and may wrinkle. An alternate method has been to widen the ends slightly for 1 cm. beyond the actual anticipated length and sew the lateral seam without including a cuff. In this way the excess ends are of slightly greater diameter than the diameter of the required graft, and cuffs of variable lengths can be turned at the time of implantation (Fig. 3). Still another method has been to sew a straight lateral seam and to cut the ends to proper length with a heated metal edge so as to fuse the threads and prevent fraying of the fabric (Fig. 3). This is easily accomplished, since the melting point of nylon and Dacron is 480 F. Although the latter technique has been satisfactory in animals, we have not as yet depended on the heat method in patients. In experimental work, we have also found it possible to avoid fraying of taffeta fabrics at the cut end by impregnating the cloth with collodion at the proper length and cutting the material after the collodion has dried. We have experimented with grafts prepared by heat sealing the lateral seam but do not believe this seal to be reliable (Fig. 3). If insufficient heat has been used, the seam separates under pressure, and if too much heat has been used the threads of the fabric are weakened or destroyed at the seam.

In the construction of a bifurcation graft two layers of the fabric are pinned together and the pattern is outlined on the cloth after it has been drawn correctly on paper. The lateral seams are sewn as already described, as are the medial seams on the limbs. The excess cloth is then trimmed, leaving at least 4 mm. outside the suture lines to prevent loss of the line because of fraying. The ends may be prepared by the methods already described. If the angle of bifurcation is incorrect the graft may buckle at the crotch.

Because of the possible presence of soluble additives which might be toxic to mammalian tissues, all fabrics should be boiled in a detergent solution for 30 minutes before use. Since nylon, Dacron, and Orlon are stable to 455 F, it is possible to autoclave these materials for sterilization without stiffening, loss of strength, or shrinkage. Vinyon-N

cannot be exposed to this degree of heat without significant changes. In some additional experiments, a woven seamless tube * of 400 denier multifilament nylon yarn was implanted into the thoracic aorta and superior vena cava, (Figs. 4*A* and *B*.

Technique of Implantation.—Since diseased arteries and synthetic fabric have minimal elasticity, exactitude in matching the diameters is of importance. In general, a traction suture of 00000 braided nonabsorbable surgical (silk) suture is used to approximate the replacement at its lateral seam to the vessel. Another suture is then placed equidistant along the circumference, to effect two-point traction. By elevating the graft it is possible to complete the posterior anastomosis with a continuous row of 00000 braided silk sutures. The anterior anastomosis is accomplished in the same manner. The sutures are passed through the fabric at least 2 mm. from the edge and approximately 2 mm. apart. Closer stitches appear to be required for a blood-tight anastomosis than with tissue grafts. Should a wrinkle develop because of inadvertent disproportion, an additional suture in the anastomosis may minimize the defect. The edge of the fabric should be handled gently with smooth forceps, since toothed forceps or crushing clamps across the fabric may cause damage. In one clinical case a Kelley clamp was placed across one iliac limb of a bifurcation replacement; consequently blood flow could be reinstituted through the aortic portion of graft and the other iliac while the final anastomoses were being completed in the excluded iliac limb. Bleeding occurred several hours after operation, and at exploration blood was leaking from the two points in the seam across which the clamp had been placed.

Blood is allowed to flow into the replacement by removal of the distal clamp first. When fabrics with a porosity of less than 16 are used, there is generally only a sweating of blood through the cloth. Bubbles trapped under the top layer of fabric may easily be removed by puncturing the cloth with a fine hypodermic needle. Most of the blood loss occurs at the anastomoses and lateral seams. After less than a minute the proximal clamp can be safely removed. In aortic resections full blood flow should be reestablished slowly, so that a profound hypotension will not ensue. Use of a pressor drug and rapid administration of whole blood by the intravenous route is helpful at this time. When a fabric with a porosity of more than 20 is used, significant bleeding may occur through the fabric. It may be expedient to wait one or two minutes before removing the proximal clamp. With very porous fabrics preclotting may be necessary. During preparation of the graft site, the fabric is placed in an area in which blood may pool, as in the pelvis, or else the graft can be placed in a glass or rubber tube containing the patient's blood. Gross clots are milked from the graft at the time of implantation. This method has theoretical disadvantages and dangers over the use of less porous fabric, especially when the graft is of small diameter.

* Obtained from Ethicon Suture Laboratories, New Brunswick, N. J.

RESULTS WITH EXPERIMENTAL AND CLINICAL SYNTHETIC REPLACEMENTS

Experimental Studies

Adult mongrel dogs with an average body weight of 15 kg. were used in this study. Anesthesia was achieved with intravenous pentobarbital sodium (Nembutal) in a dosage of 30 mg. per kilogram of body weight. When open thoracotomy was required, respiration was controlled by a Rand apparatus. During most of these procedures, ether and oxygen were used to supplement the barbiturate. At the completion of intrathoracic operations 100,000 units of penicillin were instilled into the chest. In all animals the drug was given subsequently by the intramuscular route for about a week. No anticoagulant drugs were used.

There were 41 implantations of synthetic fabric tubes in the vascular system of dogs, with an observation period of up to one year. In addition, the woven seamless nylon tube was implanted into the thoracic aorta of three dogs (Fig. 5*A*). These have functioned well for over six months. A segment of artery approximately 75% of the length of the replacement was resected before implantation. During the follow-up period, function of the graft was checked by palpation of the distal pulses, clinical condition of the animal, and by periodic visualization studies.

Nineteen fabric tubes were implanted into the thoracic aortas of 18 dogs. In one animal 3.0 cm. grafts were implanted into the upper and lower descending thoracic aorta, with an interposed segment of normal aorta. A Dacron fabric was used for both, but in one the yarn was siliconized. The function of both was excellent through six months of observation. Of the remaining 17 replacements of the thoracic aorta, there has been excellent function in 16. In one there was reduction of lumen by a mural thrombosis, of about 20%. This was observed at autopsy 75 days after operation. The longest period of observation in this group has been one year.

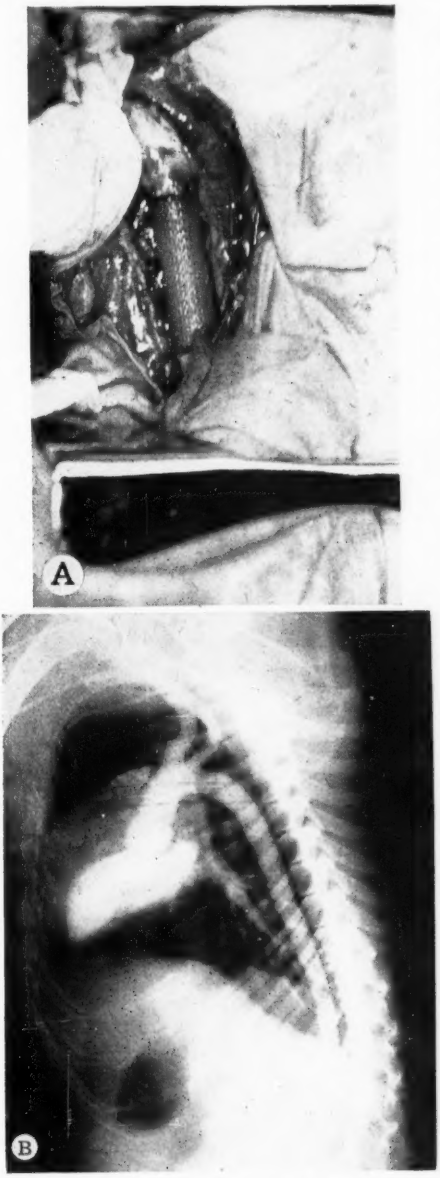


Fig. 5.—*A*, woven seamless tube of nylon functioning in the thoracic aorta of a dog at time of implantation. *B*, aortogram at four months.

Seven fabric grafts were implanted into the abdominal aorta of dogs, distal to renal arteries. Function was satisfactory in all during periods up to a year of observation (Fig. 6). However, in one Dacron fabric replacement there was a mural thrombosis reducing the lumen by about 50% at the time of autopsy, six months after implantation. In a nylon taffeta graft there was a mural thrombus which reduced the lumen by 15%. This was confirmed by autopsy eight months after implantation.

Only the low-porosity fabrics of nylon and Dacron were used in the peripheral arteries. Three grafts were implanted into the carotid artery and three into the femoral artery of the same animals. Two of the three dogs were killed at four months, and in one there was excellent function of the carotid and femoral grafts. In the other animal a 20% reduction in the lumen by thrombosis was found in both peripheral vessels, arising at the proximal suture line in each. Function appears to be excellent in both arteries of the surviving dog.

Twelve fabric tubes were implanted into the superior vena cava of dogs. Of these

Fig. 6. Aortogram showing a graft of Dacron taffeta functioning in the abdominal aorta of a dog for one year.

six were of Dacron taffeta and three were of low-porosity nylon taffeta. Intraluminal thrombosis was significant in six of the nine, being complete in two. These grafts had been in contact with empyema fluid in moribund animals. In the three grafts with partial occlusion there was a 50% reduction in the lumen of the graft and an 80% occlusion at the suture line nearest the auricle. In the remaining three dogs function appears to be excellent, as judged from visualization, clinical signs, and measurement of pressure in the jugular vein. The successes and failures were equally distributed between the Dacron and nylon replacements. Three woven nylon seamless tubes were implanted, but all failed within the first month after implantation.

Gross and Microscopic Appearance.—After the reestablishment of blood flow through a permeable fabric replacement, there is a momentary leakage of blood through the material. Fibrin and cellular elements are readily enmeshed in the fine interspaces between the filaments of the yarn, and as the natural clotting mechanism is instituted clot forms in the larger interspaces between the threads. The deposition of formed clot is generally limited by the swift flow of the blood through the graft (Figs. 7*A* and *B*). On occasion, excessive thrombosis may occur as a result of wrinkles or buckling. This is especially likely to occur if there is a slowing of blood flow and turbulance. The success of synthetic replacements in the superior vena cava was much less than that observed in the aortic replacements, probably because of lower pressure and rate of blood flow.

Within a very short time, the lining clot is infiltrated by fibroblasts, which seem to arise from the surrounding tissues. These cells pass through the interstices of the fabric into the luminal clot layer. The latter is soon organized into a compact layer, smooth and continuous with the intima of the adjacent artery to which the fabric was sewn (Figs. 7*B* and *C*). The time required for the development of an intimal zone may depend on the porosity of the replacement. Ultimately there is a thin fibrous lining inside the fabric, with either modified fibroblasts or true endothelium as a surface layer. Certain intimal cells may be derived from the blood circulating through the graft. During a period of observation of one year, there have been no noticeable degenerative changes in the fabrics of nylon or Dacron yarn. None have been recognized in dogs by Voorhees at three years in fabric replacements of Vinyon-N yarn. Although the thickness of the investing layer decreases with time, there is no evidence at the present time which would indicate that the synthetic fabrics undergo any significant alteration when functioning in the vascular system for periods of time of from one to four years. However, Shumacker and also Wesolowski have observed cholesterol deposition and even calcium in the intimal zone of fabric replacements of nylon and of Orlon. We have observed a cholesterol deposit in the intimal zone near the midportion of one nylon graft at one year.

Clinical Cases

Our experience with nylon and Dacron taffeta fabrics in 20 human cases has been very satisfactory, although the follow-up period is nine months at the most. Replacement of the bifurcation of the abdominal aorta was performed in 12 cases. Arteriosclerotic aneurysm was the diagnosis in all but one. In this patient resection was performed for thrombotic occlusion. There was subsequent occlusion of the right iliac limb of the Dacron graft, but without serious sequelae. At the time of the resection, marked atheromatosis of the peripheral vessels was noted, and a limited intimectomy had to be performed to permit anastomosis of the iliac arteries to the graft. Visualization had revealed diffuse occlusion of the smaller arteries in the leg of this man prior to operation.

In two additional patients, there was simple tubular replacement of the abdominal aorta for arteriosclerotic aneurysm. In one, there was a walnut-sized sacculation, for which a tube of nylon fabric was sufficient replacement (Figs. 8*A*, *B and C*). In the other, a young woman, there was a fusiform

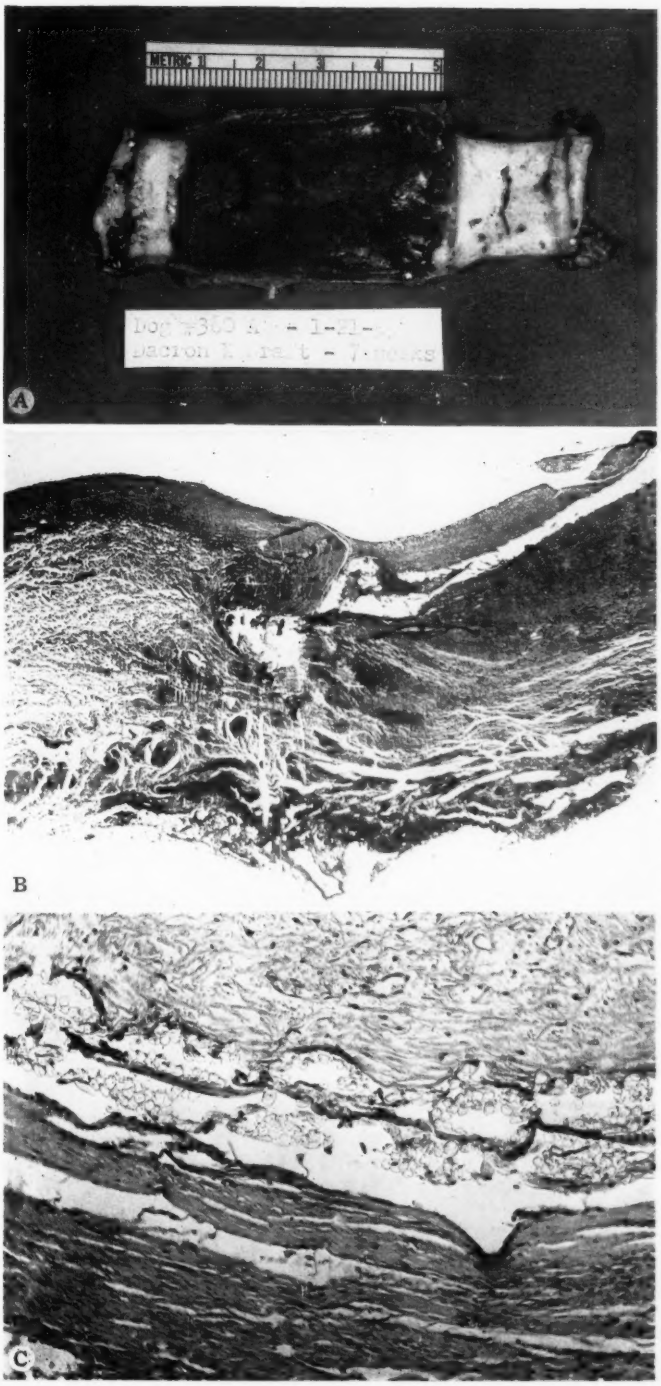


Fig. 7.—*A*, graft of Dacron taffeta fabric in thoracic aorta of dog for seven weeks. Initially fibrin clot coats the inner surface. Infiltration of this layer by fibroblasts through the interspaces of the fabric produces an intima. *B*, anastomosis of a nylon taffeta graft to abdominal aorta (at left) shown at two months. The intimal zone of the replacement joins that of the aorta without interruption. Outside the layer of nylon there is a firm thick fibrous adventitial zone. The nylon fabric was removed before the sections were cut. Hematoxylin and eosin stain; reduced from mag. × 30. *C*, photomicrograph of Dacron taffeta graft at three months. The organizing clot forming the new intima is shown at the top. The fabric is shown with occasional fibroblasts between the filaments of Dacron yarn, appearing to arise from the well-organized adventitial fibrous tissue below. Hematoxylin and eosin stain; reduced from mag. × 150.

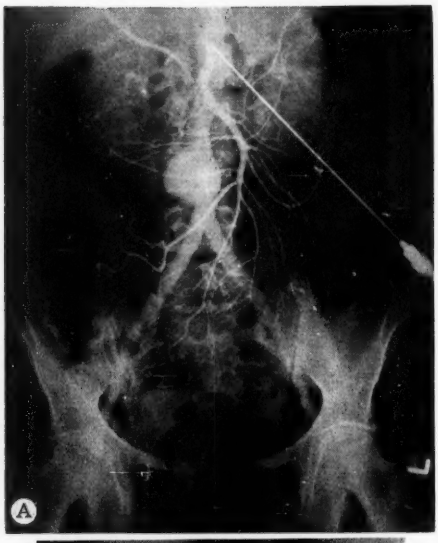
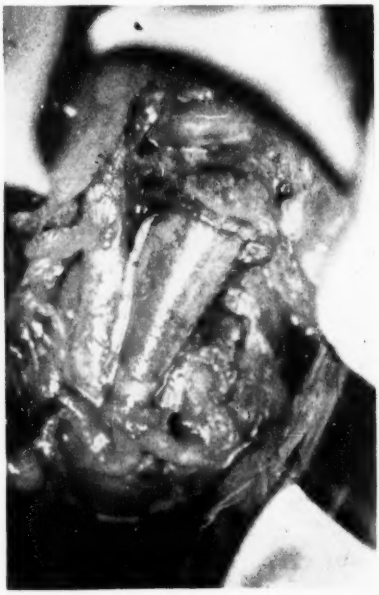


Fig. 8.—*A*, aortogram reveals localized saccular arteriosclerotic aneurysm of abdominal aorta. *B*, aneurysm at time of operation. *C*, tubular replacement by nylon taffeta fabric prosthesis.

Fig. 9.—Replacement in abdominal aorta following resection of arteriosclerotic aneurysm. Note the unusual shape and size of the graft. A calendered taffeta of Dacron was used.



aneurysm involving the entire descending thoracic aorta and infrarenal portion of the abdominal aorta, to within a centimeter of the bifurcation. Distal to this the arteries appeared to be normal. She had no history or positive tests for syphilis. An unusual graft was required, being only 5 cm. in length and reducing in width from 3.6 cm. proximally to 1.5 cm. at the distal end (Fig.

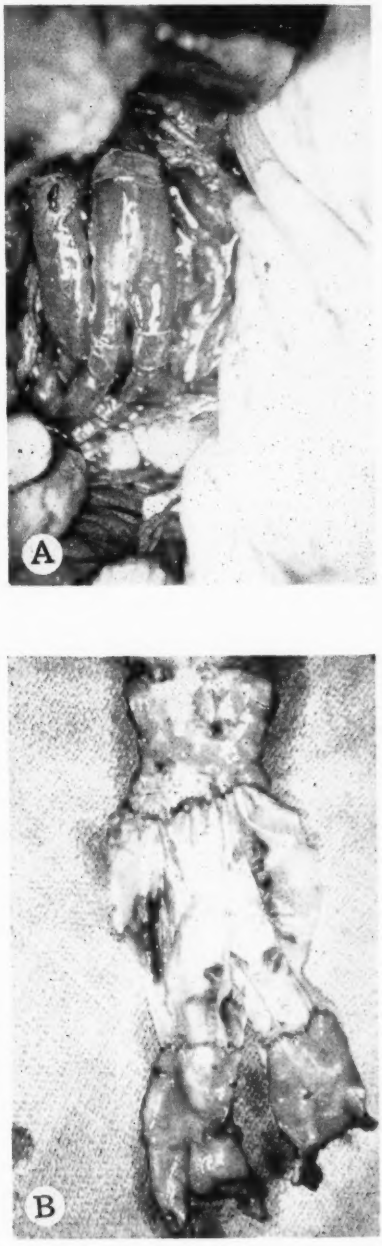


Fig. 10.—*A*, aortic bifurcation graft of nylon taffeta fabric functioning well after excision of an arteriosclerotic aneurysm. *B*, the condition of the graft was satisfactory 12 hours after implantation. Death of the patient was from massive atelectasis.

9). There has been excellent function in both of these patients.

In the aortic aneurysm group there were two deaths in the immediate postoperative period. One patient's aneurysm ruptured four days before admission, and cardiac arrest occurred at the time of emergency exploration. Heart action was reestablished, and the aneurysm was successfully resected and replaced with a nylon fabric. However, the patient succumbed 24 hours later to renal failure and shock. In the second case there was sudden death from massive atelectasis 12 hours after operation. At autopsy the graft was in satisfactory condition (Fig. 10). The remaining grafts have retained excellent function.

Nylon fabric replacements have been used in two patients in whom there were fusiform aneurysms of the upper portion of the descending thoracic aorta. One patient had a cardiac arrest before completion of the implantation. Although the procedure was completed, the patient did not survive. In the other, a 15 cm. replacement was implanted after insertion of a bypass of nylon fabric measuring 2.5 cm. in diameter. Despite excellent function of the bypass during resection of the intervening aortic segment and implantation of the graft, the patient had a transverse myelitis of the spinal cord. The graft has functioned very well, however.

Fabric replacement in the femoral artery has been employed in only three limbs by us. In one there had been incipient gangrene in the toes and diffuse occlusive disease in the small vessels of the leg below the knee, as well as a segmental block of the femoral artery. A Dacron graft thrombosed within four hours and had to be reexplored. An attempt to remove the clot was followed by only transient success. Factors contributing to this failure were the marked degree of vascular disease distal to the implant and the fact that a somewhat unsatisfactory end-to-side anastomosis of the graft had been made to a diseased common femoral artery. In the other two patients the results have been satisfactory.

In our department McAllister has employed the same materials in eight replacements of the abdominal aorta, all of them bifurcations. There has been satisfactory function in all. He has implanted six grafts of nylon or Dacron taffeta in femoral and popliteal arteries for thrombotic occlusion.[3] There were two failures from thrombosis, but in these patients there was evidence of advanced disease peripherally. In only rare instances does thrombotic occlusion of a peripheral artery replacement lead to gangrene. This appears to result if large collateral arteries are sacrificed at time of implantation or if there has been progressive occlusion of the small distal arteries. It is of particular interest that there have been two femoral and two popliteal replacements by these synthetic fabrics which have crossed lines of active flexion. Their function has remained satisfactory for periods of more than six months.

COMMENT

Previous experience with synthetic materials in the mammalian body has been very satisfactory in general. No untoward results have been reported from nylon filament which has been employed as suture material for 15 years. Irritating qualities occasionally attributed to a synthetic material often are due to extraneous materials. The inflammatory response to dicetyl phosphate, which was employed in the processing of polyethylene, is an example. It is for this reason that we urge the surgeon who uses synthetic fabrics in clinical cases to know the specific characteristics of his material and to have a reliable source, so that he can obtain the identical fabric at a future date. By treating the cloth with a hot detergent solution before use, one can rid the yarn of volatile oils and soluble additives which might prove irritating or toxic. The presence of these agents may contribute to thrombosis, deposition of calcium, or other undesirable sequelae.

Insofar as carcinogenesis is concerned, the synthetic materials in fabric form appear to behave differently from the film. Oppenheimer and Oppenheimer [4] began a study several years ago evaluating the carcinogenic activity of several synthetic materials. To date, none has been observed with Vinyon-N, nylon, or Dacron fabric in selected strains of mice and rats, although there is a significant incidence of sarcoma when these materials are implanted in the abdominal wall as impermeable film.†

The experimental and clinical experience of Blakemore and Voorhees ‡ with a taffeta of Vinyon-N used in the arterial system has been very satisfactory. In dogs observed for four years and patients followed for two years, the fabric prostheses have demonstrated no greater incidence of thrombosis than would be expected with homografts. Fabric replacements in animals studied microscopically at three years by Voorhees have shown no evidence of deterioration, in contrast to the changes which developed in homografts.[6] Tests of tensile strength at two years showed no significant losses with Vinyon-N replacements.§ Although we believe that other synthetic materials may be superior to Vinyon-N and prefer a less porous cloth than the original taffeta employed by Voorhees, Jaretski, and Blakemore, their fabric has stood the test of time so far. With shorter periods of observation, Hufnagel and his associates || have found that Orlon taffetas function very well, as have Wesolowski and Sauvage.[9] We are currently evaluating an Orlon taffeta with Wesolowski but have no basis yet for believing this material to be superior to the others.

Shumacker [10] and DeBakey [11] and their coworkers have explored the use of plastic coating of nylon fabric and braided tubes for arterial substitution. Even these impervious prostheses can function well, if implanted under proper conditions. We believe that porosity of the fabric may be of real value, although we have little evidence to indicate

† Oppenheimer, B. S.: Personal communication to the authors.

‡ Blakemore, A. H., and Voorhees, A. B.: Personal communication to the authors.

§ Voorhees, A. B.: Personal communication to the authors.

|| References 7 and 8.

that there is a critical pore size. Himmelstein and Ravich,¶ working for 18 months with the double-calendered Dacron taffeta used in our experiments, have also demonstrated the growth of fibroblasts between the filaments of the yarn, despite low porosity. Perhaps this infiltration can occur more rapidly if the porosity is greater. Nevertheless, the functional results with the fabrics we have tested, with relatively low porosities, have not been inferior to those with the original Vinyon-N taffeta, which had a high porosity. The importance of permeability was recognized in a previous study of materials to be used for external support of vessels [12] and has been well demonstrated recently in an experimental study by Egdahl and coworkers.[13] Using vein-lined tubes of polyethylene in peripheral veins of dogs, they showed that a high percentage thrombosed if impermeable tubing was used, whereas few failed if the tubing was perforated. Previous failures by others with solid tubes of plastic materials as well as with those of glass and metals suggest that porosity is of real importance.

It would seem that flexibility and adaptability to the dynamic stresses in the vascular system are additional characteristics of fabrics which favor continued function. Notwithstanding, our trial of synthetic materials in the superior vena cava has so far revealed them to be disappointing.[14] This calls attention to the factors of intravascular pressures and volume and speed of blood flow in respect to sustained function of the graft. The failures in peripheral vessels as compared with the excellent results in the aorta of clinical cases and animals suggest that diameter and perhaps length of the replacement are additional factors which influence success or failure. Finally, in clinical cases in which replacement of the femoral or popliteal arteries is contemplated, one must ascertain if there is obstruction of blood flow beyond the segment to be replaced. The lack of adequate arterial circulation distal to the site of grafting may cause failure, regardless of what type of replacement is used.

We have considered a taffeta weave to be superior among the flat fabrics because of the smooth surface which can be produced with this type of construction. However, the importance of this may be of limited significance, since we did not observe any greater success with the calendered Dacron than with uncalendered nylon taffetas of the same range of porosity or of the same thread count. Furthermore, there is a high incidence of success being achieved in arterial replacement with braided tubes # in which there is a coarse surface texture and very low porosity. Good function has also been reported with crimped nylon tubes, in which there is a corrugated surface.[15] We believe that greater strength is inherent in the taffeta weave or braid than with tulle weave or knits, since stress is propagated against a relatively straight segment of yarn, rather than against looped or knotted thread. In an earlier study [12] we selected a nylon tulle net to be used for external support of grafts. Although two years of observation showed satisfactory results with this type of material, we subsequently observed a breaking of the nylon filaments at the knots in a few animals. It has been demonstrated that in a synthetic fiber the loop strength is lower than that of the straight filament. Because of the ceaseless stresses in the arterial system, one should have ample strength in the synthetic replacement. We believe there is sufficient strength in the fabrics of 70-denier yarn reported herein and doubt that more than one layer is necessary, as suggested by Poth.*

Although we have been distressed at the progressive degenerative changes which can be observed in homografts implanted in dogs for periods longer than three years,[6] we do not believe the ultimate has been achieved yet in synthetic replacements or that the arterial homografts should no longer

¶ Himmelstein, A., and Ravitch, M.: Personal communication to the authors.

References 7, 8, and 15; Voorhees, A. B.: Personal communication to the authors.

* Poth, E., in discussion of Deterling and Bhonslay.[2]

be used. The experimental trial of synthetic fabric has been of short duration, with the possible exception of that of Voorhees. The seamless braided tubes have had an even shorter period of study. These tubes have a heavy surface texture, greater thickness, lower porosity, and unvarying diameter. Such features may be unsatisfactory under certain conditions. On the other hand, such tubes have more elasticity, at least initially, than that observed with taffeta fabric. Whether less desirable features are worth the omission of a seam is questionable. We have not yet observed failures of taffeta replacements to result from the presence of a seam. Most thromboses have related to disproportion, interference with smooth blood flow, defects in the anastomosis, or lack of an adequate arterial system distally. The value of prefabricated sizes may also be limited, since at times we require an odd size or shape in a replacement that would not have been available from a commercial source. We would caution against a premature enthusiasm for any materials proposed for clinical use which have not had adequate testing. If there were no other replacements available, the use of new materials under emergency conditions might be condoned. However, it appears that synthetic materials of uncertain pedigree are being used without proper testing or knowledge, in some cases because of the cost or difficulty in establishing an arterial bank.

Although we are satisfied with the synthetic fabrics which have been reported here, we are continuing our studies of the fabrics, tubes, and homologous arterial grafts. As we review the combined experience at Columbia Presbyterian Medical Center of Blakemore, McAllister, and ourselves in more than 70 clinical cases in which a synthetic taffeta fabric has been used for arterial replacement, we must conclude that the results have been gratifying.

At the present time, we are testing a new type of woven fabric tube † in conjunction with Ormand Julian, of Chicago. By use of special equipment, tubes and bifurcations of varying sizes have been woven of 70-denier Dacron multifilament yarn. The resulting taffeta has low porosity, and the woven lateral seams are barely discernable. This type of seam has the same strength and porosity as the actual fabric, in contrast to those produced by heat sealing or by sewing. It is possible that the theoretical advantages of woven fabrics and of seamless tubes may be unified in these replacements.

† Supported by the Titus and Ethyl Haffa Cardiovascular Fund.

SUMMARY

Interest in synthetic fabric replacement of blood vessels has increased, in view of difficulties in obtaining satisfactory homografts. The present study analyzed the functional results with 41 replacements in the aorta, peripheral arteries, and superior vena cava of dogs, as well as with 3 implantations of a woven seamless tube, over a period of one year. Very satisfactory performance was observed with taffeta fabric grafts of nylon and of Dacron and with the woven tube of nylon when the replacement was of the arterial system. Less success was noted with replacements of the superior vena cava. A combined experience with more than 70 grafts of synthetic fabric in the aorta and peripheral arteries of human cases at Presbyterian Hospital has been very encouraging, with a follow-up of up to two years.

Ethicon Suture Laboratories and Mr. Sol Lamport, of Alexander Lamport & Bros., provided assistance for this study. Miss Daisy Mapes assisted in the experimental laboratory, and Lewis Koster supplied the photographic reproductions. The suture material was donated by J. A. Deknatel and Son. Drs. Ellis and Hayes performed the visualization studies of the animals.

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DISCUSSION

On Papers by Drs. Lary and Meine and Deterling and Bhonsley

Dr. N. Rosenberg, New Brunswick, N. J.: I thought it might be interesting to show another material on which, in collaboration with the members of the Johnson and Johnson Research Foundation, we have been working during the past year and which we will present in greater detail at the American College of Surgeons meeting in the fall. Considering previous reports on vascular heterografts, one realizes how convenient these things would be if they could only be made to work uniformly. Accordingly, we have attempted to strip vascular heterografts of all foreign protein material which might be responsible for adverse reactions and have done this by an enzymatic process. The first slide shows a bovine carotid which has been digested and otherwise specially treated, and you can see how white it is, how the mesh, which is almost pure collagen, is visualized. The second slide shows the inner aspect, which has a smooth lining, and you can see the outside mesh again. Incidentally, collagen has been reported in a monograph by Burton to be stronger than steel when measured in dynes per square centimeters. The next slide shows one of these implants in the aorta of a dog. This is a 5 cm. graft. We have implanted this material in over 40 dogs and will be prepared to make a preliminary report in the fall. Implants have all been pretested by inflation under 200 to 900 mm. of mercury pressure, maintained in some instances for as long as 24 hours without showing any air leaks.

Dr. Thomas C. Moore, Muncie, Ind.: I should like to comment upon the paper by Dr. Deterling and his associates. Dr. Shumacker, Dr. Harris, myself, and our associates in Indianapolis have been working along similar lines and have placed in excess of 200 pliable plastic grafts in the thoracic aortas of dogs. The majority of these have worked quite nicely.

I should like to comment in particular upon one type of material. The use of this material was discussed at the spring meeting of the Society of University Surgeons by Dr. W. Sterling Edwards, of Birmingham, Ala. Dr. Edwards was kind enough to send us some of this material for use in our laboratory and some for use in clinical application. This material is a seamless type of graft produced by the Chemstrand Corporation. It is a nylon type of material which has been fixed in formic acid and siliconed. The crimping at the ends is for use either in the bypassing, end-to-side, type of anastomosis or in areas where flexibility is desirable, such as the popliteal space. We are utilizing this material in the thoracic aorta of dogs. Our standard length has been 5 cm. This type of graft has been placed

in 17 animals. Three of these animals have died or have been killed. In all of them the graft had remained patent. The grafts in the 14 living animals appear to be functioning well. This material has, it seems, certain advantages over the pliable material.

The pliable materials used by Dr. Deterling and in many of our experiments require a very meticulous type of suture technique in order to avert serious leaking at the suture line. The Edwards type of graft can be placed in the aorta readily and with good hemostasis. Our usual time for both anastomoses in the thoracic aorta was about 9 to 11 minutes. This was about one-third the time required for placement of the more pliable type of graft materials. It is quite easy to work with. Dr. Edwards, in his original paper, suggested the use of a small strip of nylon around the suture line to prevent leakage. We have found that this is not necessary. We do believe that it is important in placing the graft that the suture be passed from the aortic side into the graft and that the assistant keep tension on the suture at all times in order to maintain the elastic vessel securely approximated to the more rigid graft. When one anastomosis is completed, the operator passes to the other side of the table and commences the second anastomosis. This appears to work nicely and we have found leakage to be no problem.

I have utilized grafts of this material in two patients with segmental occlusion of the superficial femoral artery. This experience is too limited to permit any conclusions concerning the usefulness of this material in patients. We are indebted to Dr. Edwards for his kindness in providing us with this material.

Dr. N. Freeman, San Francisco: Dr. Frank Leeds and I, in San Francisco, have been using Orlon grafts for replacement in the treatment of abdominal aneurysms. I should like to ask if there are any experiences with the use of anticoagulants after the insertion of Orlon grafts. We had one patient who had some trouble with the circulation distally and was given parenteral heparin four hours after operation. Severe leaking developed from the graft itself. I should like to find out if anyone else has had such an experience.

Dr. Geza de Takats, Chicago: I should like to say a few words about this steel mesh before it gets completely asphyxiated by plastics. This work was really undertaken by one of our graduate students who has since left the University, and, since the mesh had been inserted about 9 to 11 months, we thought it would be worth while to see what happened to it. It was not done with the idea that we would ever use this clinically alone. However, since it is so inert and so easy to use—it doesn't buckle, it doesn't wrinkle, it is porous and permits fibroblasts to grow through—it appeared to us that it might have some limited use as a wrapping procedure, such as Vinyon-N had also been proposed. You have seen this morning the difficulty with late dilatation of vein grafts; some of the homografts, as Deterling had reported, especially the experimental ones, have shown some dilatation. One of the places where we may use it is in endarterectomy for iliac stenosis, where we often leave a rather weak arterial segment. Here, wrapping of steel mesh around the vessel may help.

Dr. Grimson, Durham, N. C.: I should like to make a brief comment. After the initial work of Dr. Blakemore and his group, Dr. D'Angelo and I used Vinyon-N tubes in the abdominal aortas of a series of dogs. In general these worked well. However, it was anticipated that one day there would be a foreign-body reaction. One of our dogs did develop a sinus in his groin, and dissection demonstrated that it led to a sloughed Vinyon-N graft. This was removed without interfering with the collateral circulation, which gave the dog an adequate femoral pulse. With cloth tubes our main trouble has been at the suture line of the anastomosis. Partial dehiscence without massive hemorrhage has led to small aneurysmal pockets. Perhaps the homografts with their elasticity have a decided advantage, particularly when one is dealing with elastic vessels. For stiffer vessels, as encountered with a Leriche's syndrome and arteriosclerosis in general, the plastic grafts could have less disadvantage and might have an incidence of success approaching that of the elastic homografts. I myself would use a plastic material in a stiffened artery if an arterial graft was not available but would insist on a homograft that is elastic for suture to an elastic artery.

Dr. Gerald H. Pratt, New York: After performing 20 grafts, we finally had an arterial homograft which became a foreign body and came out. Dr. John Madden has told me of two other instances about which he knew. So we were interested at once in the cloth studies. Due to the kindness of Dr. Edwards, we were also permitted to use some of the nylon, made by Chemstrand Co., which was just shown on the screen. We had the Company crimp the entire length. It is our feeling that the crimp is not just to help us in suturing but that in its accordian-like action it will take some of the arterial force, which is the factor against most of the prosthetics in which there is no give against the force of the heart beat. We have performed now four clinically satisfactory replacements with this type of graft.

Dr. McAllister, New York: Dr. Deterling asked me to comment about the plastic materials used in the peripheral vessels, and this will be reported tomorrow, but I simply wanted to mention that we have four instances of plastic cloth prostheses traversing the popliteal space and two instances where these prostheses passed beneath the inguinal ligament. In evaluation of the peripheral

pulses on acute flexion in these extremities, we don't appear to have any obstruction to flow.

DR. EARLE B. MAHONEY, Rochester, N. Y.: In our experimental laboratory we have attempted to support vein grafts by wrapping them with various prostheses. In 12 experiments vein grafts were wrapped with tantalum mesh, which I presume would be very similar to the Stainless Steel mesh suggested by Dr. de Takats. In all but two of these dogs the grafts ruptured within a week or 10 days after the operative procedure. It was our opinion that the vein graft was traumatized by this rigid prosthesis, and I would be very reluctant to use any such material about a pulsatile vessel.

DR. EMILE MEINE JR., Chicago: The last speaker has pointed out something which is quite significant. Should endarterectomized vessels be reinforced with any type of rigid or semirigid material, the beating of the vessel against the material might tend to wear out the vessel; it is quite possible, however, that vessels which would need reinforcement might already be quite arteriosclerotic and therefore not have a great amount of elasticity in their walls.

DR. RALPH A. DETERLING, New York: I wish to thank the discussors. In regard to braided tubes without seams, there are two thoughts I have: First, I'm not certain that anyone has shown that failure of synthetic fabric replacements has been related to the presence of seams. I believe nobody has given enough thought to this. Certainly the high success rate observed in the larger vessels would make one believe that the value of seamless tubes might not necessarily be as important there as has been thought. Second, the thickness of the wall of any of these braided seamless tubes is greater by from two to two and a half times that of the fabrics, and, therefore, by virtue of this thickness a decrease in porosity might oppose the ingrowth of fibrous tissue. Again I don't know if this is very important. There is little question that synthetics in solid form, such as tubes of Polythene, Lucite, and so forth, were not good insofar as function, and this is considerably different from what has been achieved with synthetic fabrics. It may be flexibility, it may be porosity—I don't know. I just bring this up as a thought. I don't believe we have used heparin frequently enough with our synthetic fabric replacements to make any comments on one of the questions that came up. I personally haven't, anyway, having gotten into trouble in a few cases with homografts. I believe it is something that should not be necessary in most cases.

In regard to the Chemstrand development of a braided nylon tube, it is extremely interesting and I followed it with great interest. However, formic acid, which has been used by them, is a solvent of nylon and should further reduce the porosity. Nevertheless, the short-term follow-up has demonstrated apparent good success with them. As I recall the slides which Dr. Sterling Edwards showed in Houston in February, the crimps of his tubes were filled in with clot in Nature's effort to have a smooth flow. That is one thing I believe should be kept in mind in considering the value of crimping.

I'm certainly not against homografts, although I believe we have used only one or two in the aorta at Presbyterian Hospital in the past six months. In regard to Ivalon, we have used it as tubes with walls of 5-mm. thickness in the thoracic aorta of dogs. These all ruptured about the fourth day. We have had much better success with highly compressed Ivalon tubes. So far as external support with this material is concerned, we have no experience. Dr. Lester Vargas and I did a study a couple of years ago using a tulle weave nylon net applied about homografts. We feared that in time, if degenerative changes of homografts continued, we might get further dilatation and aneurysm. We used it in about 12 clinical cases and a large series of dogs. At two and a half to three years, though, we were disturbed to find that the net had ruptured at the knotting in about 3 of 15 dogs. In other words, the tensile strength of the synthetic fiber is much less in a knot or loop than it is in its straight length. With the fatigue effect of continuous pulsatile thrust against this external support, which was only one layer thick, there was eventual breakage of the filaments. This experience again points up the great need for long-term follow-up in this field.

Observations on Experimental Revascularization of the Kidney

A Preliminary Report

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J. WILLIAM HINTON, M.D.
JERE W. LORD Jr., M.D.
and
CHARLES G. NEUMANN, M.D., New York

In 1951 our attention was directed to the revascularization potential of a tubed pedicle flap of skin and subcutaneous tissue.[1] It has long been known by plastic surgeons that such a flap is capable of bringing new blood supply to an ischemic area on the body surface.[2] This is possible because of the development of anastomotic channels between the vessels of the flap and those of the ischemic tissues to which the flap is attached. Therefore, the flap may be thought of as a framework or strut serving, through its intrinsic vessels, to transport blood from one area of the body to another.

With these thoughts in mind, a series of experiments was undertaken to determine the ability of such a flap to bring blood to a visceral circulation. Primary interest focused on the heart because of the clinical usefulness of the procedure if such revascularization could be demonstrated. The results of these experiments have been reported elsewhere.*

Because of the great difficulty in proving that blood from the flap actually entered the coronary circulation, it was thought that a more suitable test organ than the heart might be used to determine the revascularization potential of the flap. The kidney seemed ideally suited for this purpose because its source of blood supply could be readily interrupted without causing death, numerous renal function tests such as the phenolsulfonphthalein excretion and *p*-aminohippurate clearance are available, and the kidney may be visualized radiologically after the intravenous administration of a contrast medium.

In considering the problem of revascularization of an organ, evidence indicates that the most effective stimulus for the development of collateral blood supply is ischemia of the organ. The induced ischemia must be gradual and progressive. Unfortunately, there has been no entirely reliable method of achieving this. A mechanical self-closing spring clip has been developed in our laboratory and will usually produce delayed progressive occlusion of a vessel. However, at present its rate of closure is unpredictable. We prepared a group of experimental animals and applied self-closing clips to the renal arteries, realizing that in many cases the rate of closure of the clip would be too rapid. However, it was felt that ischemia would be gradual enough in some of these animals to allow satisfactory time for the optimal development of collateral vessels between the flap and the renal cortex. In

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From the Department of Surgery, New York University Postgraduate Medical School.

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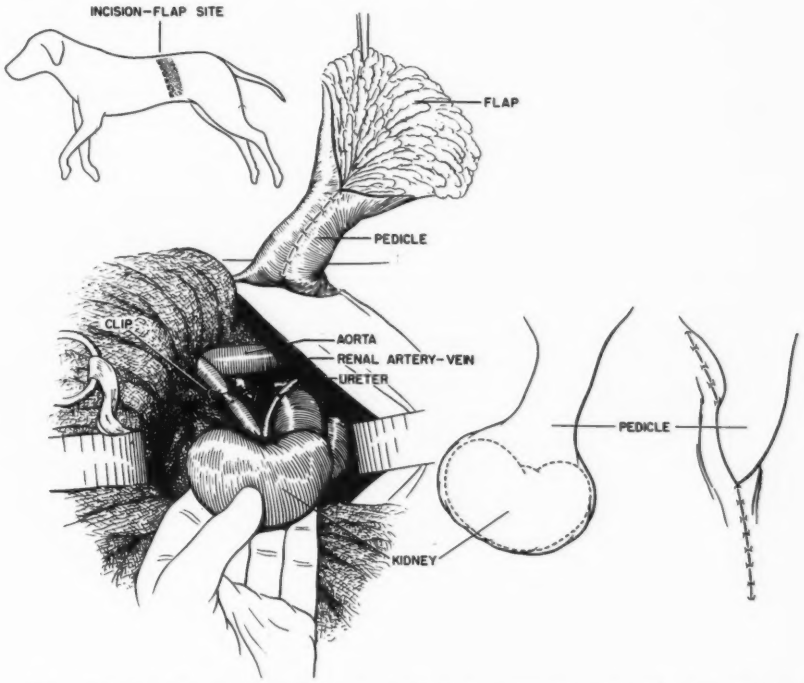


Fig. 1.—Artist's illustration outlining the method of construction and application of a tubed pedicle skin flap to the dog's kidney.

these animals the direction of blood flow through the collateral channels could be investigated.

TECHNIQUE

The experiments were performed in healthy adult mongrel dogs weighing 15 kg. on the average. They were anesthetized with intravenous pentobarbital (Nembutal), and all operations were performed with aseptic technique. A thoracicoabdominal pedicled skin flap was elevated on the left side and was tubed. Through an oblique subcostal incision on the same side, the kidney was mobilized and the renal capsule stripped from the cortex of the kidney and excised. A cuff of capsule was left at the renal hilus, to which the skin flap was sutured.

Fourteen animals were prepared. Seven dogs had the skin flap denuded of a split-thickness layer of skin 0.030 in. in thickness. In the remaining seven dogs the flaps were not denuded. In two of the animals with denuded flaps, the external or epithelial surface was placed against the renal cortex. In all other animals the subcutaneous aspect of the flap was sutured to the kidney.

In each of the animals an attempt was then made to produce progressive gradual ischemia of the kidney to which the flap had been attached. This was accomplished by applying to the skeletonized renal artery a self-closing spring clip. This device has been previously described.[5] It is made of stainless steel wire, and the jaws are held open by a bolus of 00 plain absorbable (gut) suture. The clip was placed around the renal artery so that the latter was enclosed in the clip's jaws. As the gut suture is absorbed, the jaws are permitted to close, thus producing a progressive occlusion of the enclosed vessel.

In 12 of the animals the clip was applied to the renal artery at the same time as the flap was applied to the kidney. In the other two animals three and one-half months were allowed to elapse between the application of the flap and the clip.

In seven of the animals the contralateral kidney was removed at the time of the initial operation. In the other group of seven a clip was applied to the renal artery of the contralateral kidney. The animals were studied by means of weekly determinations of the blood urea nitrogen and the blood pressure. The latter were obtained by direct femoral

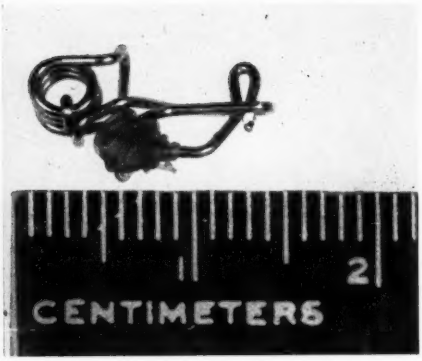


Fig. 2.—Photograph of self-closing spring clip used for the production of gradual renal arterial occlusion in the present experiments.

artery punctures, using a mercury manometer. The rate of closure of the clips was followed by means of x-rays.

RESULTS

Two animals survived complete occlusion of the renal artery to the kidney to which a flap was attached. These animals afforded unequivocal evidence of renal function. The findings in these experimental preparations form the basis for this report.

Both of these animals had flaps applied to the left kidney three and one-half months prior to the application of the clip. In one the clip closed in approximately four weeks. In the other the clip closed in six to seven weeks. The first animal (Dog 02-4) had a normal right kidney, but intravenous pyelography demonstrated definite, although diminished, function on the left side (Fig. 3). The animal was killed, and the occlusion of the left renal artery was confirmed. Gross and microscopic examination showed a relatively normal left kidney. The blood pressure was 170 mm. Hg, and the blood urea nitrogen was not elevated.

The other animal (Dog 02-5) also showed function of the left kidney after x-rays indicated complete renal arterial occlusion. Gradual occlusion of the right renal artery was then effected by the application of a clip, and intravenous pyelography showed function on the side of the flap but no function on the right side. Shortly after this, the right kidney was removed and the left renal artery and vein were ligated and divided. The right kidney was atrophic (Fig. 4). The dog had hypertension (200 mm. Hg) and elevation of the blood urea nitrogen to 30 mg. per 100 cc. Studies performed at this time showed diminshed renal function. Phenolsulfonphthalein excretion on two occasions was 27% and 28% in one hour. The specific gravity of the urine was 1.017 after maximal concentration. The urine showed a persistent 1+ reaction for albumin. Renal blood flow determinations obtained by means of *p*-aminohippurate clearance studies indicated on two occasions a renal blood flow of 96 cc./minute and 97.5 cc./minute. Two months after complete occlusion of the left renal artery, the base of the pedicle flap was severed and the *p*-aminohippurate clear-

Fig. 3 (Dog 02-4).—Four and one-half months after application of tubed pedicle flap to left kidney. Photograph of x-ray taken 20 minutes after the intravenous injection of 35% iodopyracet (Diodrast). A normal pyeloureterogram is seen on the right. Dye is also present in the left kidney four days after closure of the clip on the left renal artery. The lower four clips are in the subcutaneous tissues of the abdominal wall and were inserted for the purpose of evaluating the rate of clip closure.

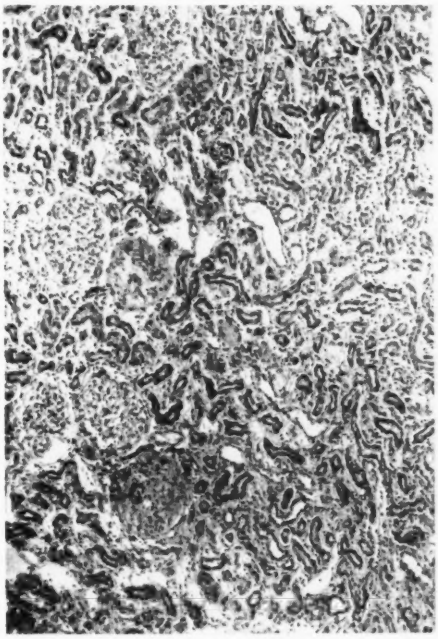


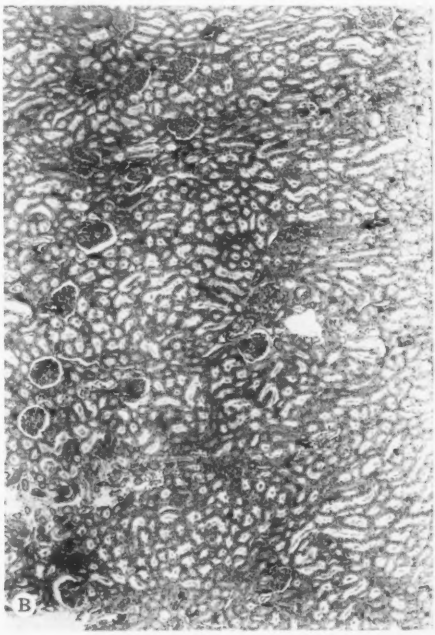
Fig. 4 (Dog 02-5).—Photomicrograph of right kidney, showing extensive hyalinization of the glomeruli. Renal arterial occlusion was effected by a self-closing clip, and no skin flap was applied to the kidney. Hematoxylin and eosin; reduced about 2/5 from mag. × 157.

Fig. 5*A* (Dog 02-5).—Autopsy specimen eight and one-half months after application of tubed pedicle flap to kidney. The kidney is split to show the adherence of the flap to the renal cortex and the normal gross appearance of the kidney.

Fig. 5*B* (Dog 02-5).—Photomicrograph of the left renal cortex. There is no evidence of infarction or extensive renal cortical atrophy. Hematoxylin and eosin; reduced about 3/5 from mag. × 55.

ance indicated that the renal blood flow had decreased to 25.5 cc./minute. The animal was killed one week later, and the left kidney appeared relatively normal grossly and microscopically (Figs. 5*A* and *B*). The reason for the persistent renal blood flow following division of the tubed base of the flap was found to be anastomoses through adhesions between the flap and adjacent tissues. It was concluded from the studies in this animal that the pedicled flap was carrying approximately 71 cc. of blood a minute into the renal circulation.

The remaining 12 animals failed to provide the proper experimental preparation for evaluation of the flap. Three of the animals died in the early postoperative period. One of these exhibited torsion of the single remaining kidney. The other two died of peritonitis within a week after operation. Both of these had undenuded flaps on the kidney, and the infection probably came from the skin surface. In eight animals the clip closed in four weeks or less, and the animals died in uremia. It is believed that closure of the clips in such a short period does not afford



time in most cases for the development of adequate blood flow through the collaterals. The one remaining animal was found to have a branch of the renal artery to which a clip had not been initially applied. Excluding the three animals who died in the early postoperative period, all the animals developed a hypertension as renal arterial occlusion progressed. The mean blood pressure varied from 170 mm. Hg to 210 mm. Hg. This is most likely a result of the renal ischemia. The blood urea nitrogen was elevated in each of the animals that died of uremia.

COMMENT

It was realized at the outset of these experiments that it would be difficult to create an experimental situation which would indicate whether blood might enter a visceral circulation from a pedicled flap of skin. The major difficulty is believed to be the inability to consistently produce a graded and controlled progressive occlusion of the renal artery over a sufficiently prolonged period.

The technique of producing gradual arterial occlusion by means of a self-closing spring clip has been a valuable laboratory procedure in the production and the study of the development of collateral circulation. However, a major difficulty has been the inconsistent rate of closure of these clips. This would seem to be the direct result of the extremely variable rate of gut suture absorption. It is important to emphasize that the spring clip will not close completely until there has been total gut suture absorption.

In these experiments the functional integrity of the kidney depends upon a balance between the rate of occlusion of the renal artery and the growth of collaterals. The latter is a slow process, and presumably, therefore, the more gradual the occlusion of the renal artery, the greater the chance of revascularization by the flap. This is in keeping with the generally observed fact that the size and number of new collateral arterioles are inversely proportional to the rate of major arterial occlusion. Unfortunately, in the present study the majority of the clips closed within 30 days. This probably represents an insufficient time interval for the maximum development of collateral channels.

The results presented do indicate, however, that under optimal conditions blood from the pedicle skin flap will enter the renal circulation. The volume of blood flow, although less than enough to maintain normal renal function, is certainly sufficient to maintain life. In the one animal evidence indicates that the flap was able to transmit 71 cc. of blood a minute to the kidney. This is a surprisingly large amount and is roughly one-third of the total unilateral renal blood flow in the normal dog.

SUMMARY AND CONCLUSIONS

An experimental study designed to evaluate the visceral revascularization potential of a tubed pedicle flap of skin is presented. This is only one approach to the complex problem of introducing a new blood supply to ischemic organs, and it would be presumptuous on our part to suggest a clinical application of this method at present. However, we feel the unusual and interesting results in some of the present animals warrant further investigation.

DISCUSSION

DR. GEZA DE TAKATS, Chicago: Mr. Chairman, I should like to congratulate Dr. Stone on a very important piece of work which was of great interest to me, and I am sorry I didn't read the program before because I should have come a little better prepared to discuss it.

In 1940, Dr. Scupham and I (de Takats, G., and Scupham, G. W.: Revascularization of the Ischemic Extremity, Arch. Surg. **41**:1394, 1940) encountered five hypertensive patients in whom we thought sympathectomies would be of no avail because their renal function was so diminished. In these patients, we sacrificed the kidney and put omentum and muscular flaps into them. I might say that a long-term follow-up of these patients, although they all died, showed that there was absolutely no detectable change in their clinical status. However, this stimulated our interest in the problem of producing some sort of experimental ischemia and seeing whether we couldn't show, either by angiograms which were just coming into use at the time or by renal function test, any effect on this ischemic kidney. Of course, as you all know,

there have been a number of such experiments done. Recently, at the University of Illinois, Dr. Meine, whom you heard speak this morning, found a very excellent and simple method of producing renal ischemia which is a bit more comparable with clinical arteriosclerosis, namely, by injecting sodium morrhuate into the renal artery with some compression which produced in certain instances an infarct and in others a tubular damage. Now the difficulty as we encountered it in our clinical cases and also in the experiment, which incidentally never have been published, is the fact that in order to get any kind of revascularization of the kidney you have to assume that you can get in a patient an aglomerular, tubular circulation. This would mean that the kidney is transformed into the type of aglomerular kidney which Dr. Oliver has shown does exist in nephrosclerosis and which some fish have. If it were possible to show that a human can exist without too much glomerular circulation, then I think that these experiments would have a clinical application.

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Temporary Circulatory Occlusion to the Brain of the Hypothermic Dog

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and
HENRY SWAN, M.D., Denver

The protective effect of hypothermia against brain damage by ischemia has been well demonstrated clinically. Interruption of the circulation for up to nine minutes in open-heart surgery [1] and occlusion of the cerebral circulation for up to eight minutes in neurosurgical procedures * have been successfully accomplished. The clinical use of hypothermia presupposes that the brain takes part in the generalized reduction of tissue metabolism with cooling. That it does so was demonstrated in 1954 by Rosomoff and Holaday,[2] who found a linear fall in cerebral oxygen consumption in the dog as the temperature was lowered from 35 C to 26 C; at 26 C a threefold reduction in oxygen consumption had occurred. It is possible, therefore, that the dog at 26 C tolerates total arrest of blood flow to the brain for a period roughly three times as long as would a normothermic animal. By using graded occlusion periods to the cerebral circulation of the normothermic and the hypothermic dog, we hoped to test this hypothesis.

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* White, J. C.: Personal communication to the authors.

METHODS

Healthy adult mongrel dogs were deeply anesthetized with pentobarbital sodium. An endotracheal tube was inserted, and the dog was hyperventilated at 60 respirations a minute with pure oxygen to produce respiratory alkalosis. Dogs of the hypothermia group were shaved and cooled, as previously described,[3] by immersion in ice water until a rectal temperature of 29 C was obtained. The dog was then removed from the bath. After 10 to 15 minutes, the rectal temperature dropped another 3 to 6 degrees, where it remained during the operations. The hypothermia temperature range was therefore between 23 C and 26 C. The normothermia group of dogs was maintained at between 35 C and 37 C.

Three methods were undertaken to produce temporary circulatory occlusion to the brains of both normothermic and hypothermic groups of dogs as follows:

Group 1.—Arterial occlusion alone was found to require a more extensive procedure than ligation of both carotids and vertebrals in the neck.† Because the large anterior spinal artery is supplied by the first five pairs of intercostals, it was necessary to ligate both the internal mammary and the aforementioned intercostal arteries. This was performed by entering the left chest through the fourth or fifth intercostal space. After this collateral supply had been interrupted, temporary occlusion of the brachiocephalic and subclavian arteries, just above the arch of the aorta, was maintained for specific periods of time (Fig. 1). To test the effectiveness of occlusion by this method, a small area of parietal cortex was exposed by trephining. After the usual vessels had been occluded in the thorax, the dura was opened and the surface of the cortex

† References 4, 6, and 12.

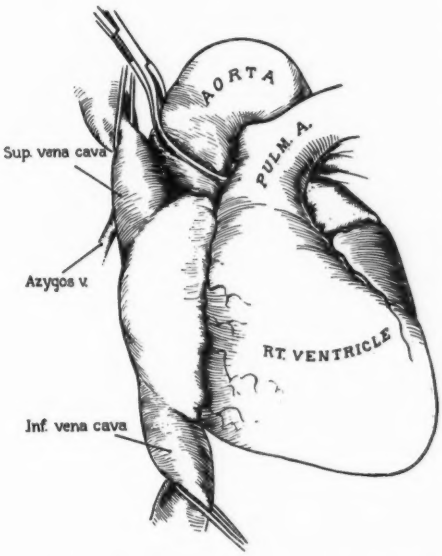

Fig. 1.—Method of producing arterial occlusion alone. Through a left thoracotomy opening, ligation of both mammary and upper five intercostal arteries is followed by temporary occlusion of the brachiocephalic and subclavian vessels.

was observed with Wood's lamp subsequent to the injection of 1 cc. of fluorescein into the aorta. Appearance of dye after injection was recorded.

Group 2.—Venous and arterial occlusion at the neck necessitated a preliminary laminectomy at the level of C-2, as described by Kabat and Dennis.[7] After a two-week recovery period from this "unroofing" procedure, total arterial and venous circulatory occlusion was accomplished by means of a pneumatic cuff applied about the neck and inflated to 600 mm. Hg in a matter of one or two seconds. Here again, specific periods of occlusion time were maintained (Fig. 2).

Group 3.—Venous and arterial occlusion at the heart simulated the procedure used in open-heart surgery,[8] except that the heart itself was protected by leaving open the azygos vein, coronary arteries, and pulmonary vessels. The right chest was incised through the fourth intercostal space. The superior and inferior venae cavae were occluded with umbilical tapes, and the aorta was cross clamped (Fig. 3).

Aseptic technique was utilized for all procedures. Those animals in which the chest was entered were closed in layers with water-sealed drainage. The hypothermic animals were placed in a warm water bath (40 to 45 C) after completion of the operation until a rectal temperature of 30 C and spontaneous respiration were obtained. Six hundred thousand units of penicillin were given postoperatively.

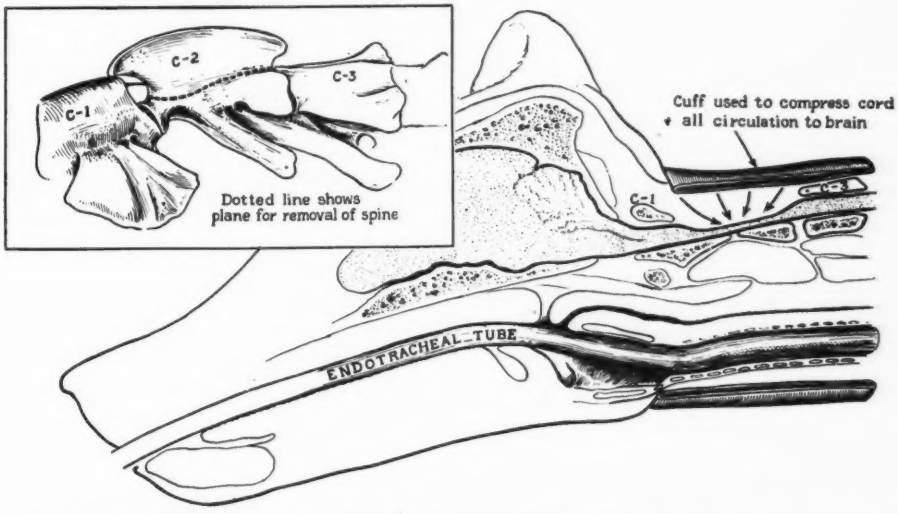

Fig. 2.—Method of producing arterial and venous occlusion at the neck (after Kabat and Dennis [7]). A preliminary laminectomy at C-2 "unroofs" the spinal cord. After recovery, a pneumatic cuff about the neck results in absolute occlusion.

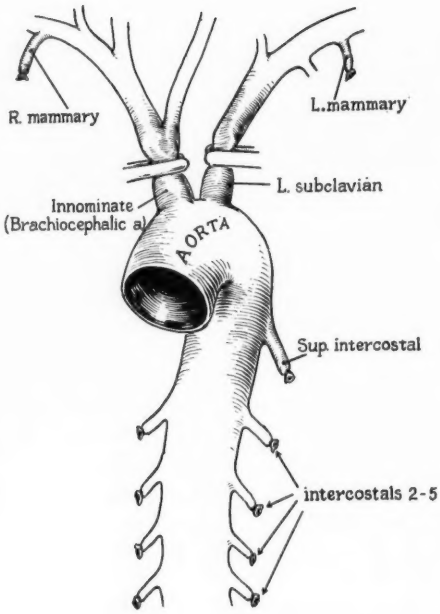

Fig. 3.—Method of producing arterial and venous occlusion at the heart. Through a right thoracotomy the venae cavae are occluded and the aorta cross clamped. The azygos vein, coronary arteries, and pulmonary circuit remain open.

The clinical behavior of the dogs after periods of temporary cerebral ischemia by all methods, as described by Kabat and Dennis,[7] fell into four groups with increasing occlusion time. With the least ischemia there followed immediate recovery and normal behavior. A second group demonstrated varying degrees of temporary ataxia, lasting up to one month, from which they invariably recovered. More profound ischemia produced permanent coma. Some of these dogs could be kept alive for a few days, but death always ensued in less than a week. Finally, those with the most extensive ischemia died within 12 hours in apparent shock. Throughout this study only dogs in the first two groups were classified as survivors.

Surviving dogs were killed from four days to three months postoperatively, and histologic studies of the brains were made in four standard areas. These included frontal cortex, parietal cortex, temporal cortex, and cerebellum. Alcohol fixation with hematoxylin and eosin and Nissl stains were carried out routinely. Detailed studies of the brains were not performed, but rather specific cerebral and cerebellar lesions were looked for and compared. Permanent late injury to these specific sites was the criterion used to define significant pathologic damage.

RESULTS

A total of 77 dogs was used for the overall experiment: 36 in Group 1, 20 in Group 2, and 21 in Group 3. Of these 77 animals, 53 survived the occlusion periods, 28 of which were used for gross and microscopic studies.

Group 1: Arterial Occlusion Alone.—Thirty-six dogs underwent temporary occlusion of the brachiocephalic and subclavian arteries after interruption of the aforementioned collateral circulation. In 21 of these occlusion was produced during normothermia for 6 to 30 minutes. The remaining 15 dogs were subjected to occlusion periods during hypothermia of 10 to 60 minutes. By this method dogs survived occlusions to 15 minutes at normothermic temperatures and 45 minutes during hypothermia (Table 1). This threefold prolongation of occlusion time with survival was borne out by

TABLE 1.—*Occlusion Times and Survival Results by Arterial Occlusion Alone (Group 1)*

Normothermia (35-37 C)				Hypothermia (23-26 C)			
Minutes	No. Dogs	Lived	Died	Minutes	No. Dogs	Lived	Died
6	1	1	..	10	1	1	..
10	4	4	..	20	3	3	..
12	3	3	..	30	4	4	..
14	3	3	..	40	1	1	..
15	3	2	1	45	3	2	1
16	1	..	1	50	1	..	1
18	1	..	1	60	2	..	2
20	2	..	2	..	..	..	..
25	2	..	2	..	..	..	..
30	1	..	1	..	..	..	..

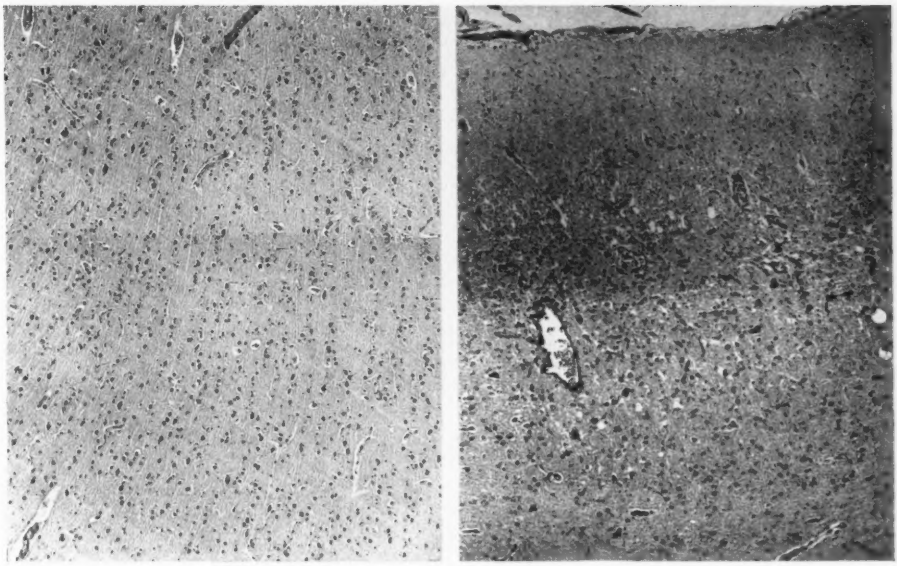

Fig. 4.—Arterial occlusion alone. Left, 30 minutes' occlusion during hypothermia; the dog was killed after five days. Cortex almost normal. Right, 14 minutes' occlusion at normal temperature; the dog was killed after two weeks. Photomicrograph shows early band-shaped necrosis with loss of neurons, vasodilation, vascular and glial proliferation involving middle and lower cortical layers. Reduced about ⅕ from mag. × 100.

pathology studies in seven dogs killed in this group. Significant permanent damage occurred at 10 minutes in the normothermic animals and at 30 minutes in the hypothermic group (Fig. 4).

Nineteen dogs in this group were subjected to trephining and cortical inspection after fluorescein injection. In 12 of these the dye was seen in the cortical vessels at some time prior to release of the occlusion. In spite of this no difference in the tolerance of the two groups to occlusion could be found, and the survival results throughout were quite consistent.

Group 2: Venous and Arterial Occlusion at the Neck.—A preliminary "unroofing" laminectomy was successfully performed on 20 dogs. The pneumatic-cuff technique which produced absolute arterial and venous occlusion was used on 10 normothermic dogs for periods of 2 to 10 minutes and on 10 hypothermic dogs for 6 to 16 minutes. Death occurred after 6 minutes in the normothermic group and after 12 minutes in the hypother-

TABLE 2.—*Occlusion Times and Survival Results by Arterial and Venous Occlusion at the Neck (Group 2)*

Normothermia (35-37 C)				Hypothermia (23-26 C)			
Minutes	No. Dogs	Lived	Died	Minutes	No. Dogs	Lived	Died
2	2	2	..	6	1	1	..
4	3	3	..	8	2	2	..
6	2	2	..	10	2	2	..
8	2	..	2	12	2	2	..
10	1	..	1	14	2	..	2
..	..	..	..	16	1	..	1

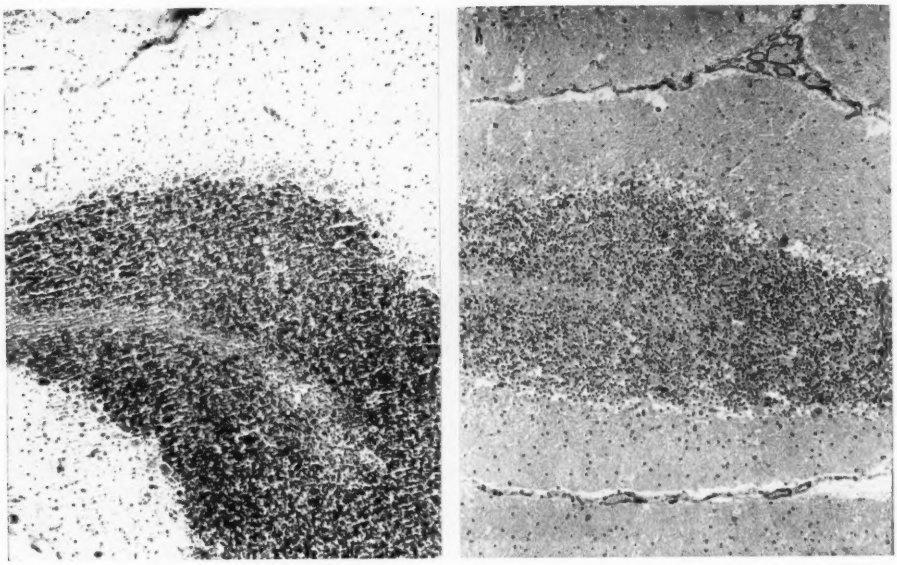

Fig. 5.—Arterial and venous occlusion at the heart. Left, 12 minutes' occlusion during hypothermia; the dog was killed after eight days. Normal cerebellar cortex. Right, 12 minutes' occlusion at normal temperature; the dog was killed after 11 days. Photomicrograph shows loss of Purkinje cells, edema of Purkinje-cell layer, disappearance of numerous granular cells. Reduced about ⅕ from mag. × 100.

TABLE 3.—*Occlusion Times and Survival Results by Arterial and Venous Occlusion at the Heart (Group 3)*

Normothermia (35-37 C)				Hypothermia (23-26 C)			
Minutes	No. Dogs	Lived	Died	Minutes	No. Dogs	Lived	Died
2	1	1	..	4	1	1	..
4	1	1	..	7	1	1	..
6	1	1	..	10	1	1	..
8	1	1	..	14	2	2	..
10	2	2	..	16	1	1	..
12	2	..	2	20	2	2	..
14	1	..	1	22	1	1	..
..	..	..	..	25	2	..	2
..	..	..	..	30	1	..	1

mic group (Table 2). Nine surviving dogs were killed for brain studies. Significant pathologic changes occurred between 4 and 6 minutes in the warm animals and between 10 and 12 minutes in the hypothermic group.

Group 3: Venous and Arterial Occlusion at the Heart.—As in the previous procedure, a twofold increase in occlusion time was achieved by hypothermia in this group. A total of 21 dogs was subjected to caval and aortic cross clamping, 9 during normothermia, with occlusion times of 4 to 30 minutes. The normothermic animals tolerated occlusion to 10 minutes, while during hypothermia the venous and arterial obstruction period was prolonged to 22 minutes (Table 3). Twelve of the 15 survivors in this group were killed. Permanent microscopic brain damage was seen at 8 minutes in the warm animals and by 14 minutes in those subjected to hypothermia (Fig. 5).

COMMENT

The three methods described in this study were chosen primarily because they were found to yield consistent results. Experimental occlusion of the blood supply to the brain has interested physiologists, anatomists, pathologists, and surgeons for many years. In 1836, Sir Astley Cooper [4] ligated both carotids and compressed the vertebral arteries in a rabbit, with resultant death. He subsequently ligated these four vessels in a dog with no ill effects. Killing of this animal for examination after three months revealed extensive anastomoses in the neck from the upper intercostal arteries. Leonard Hill,[5] in 1896, performed similar experiments and demonstrated the rich and variable collateral network of the upper intercostals with the anterior and posterior spinal arteries in dogs. Rabbits, cats, and dogs were all found to yield inconsistent results on permanent ligation of the brachiocephalic and subclavian arteries alone. These same collaterals were later demonstrated roentgenologically by Andreyev.[6] The method which we utilized in creating pure arterial occlusion to the brain was a logical outgrowth of this previous work.

The fluorescein studies during occlusion in this group failed to demonstrate absolute occlusion in 12 of 19 dogs tested. In spite of the consistent survival results, therefore, total arterial occlusion was not uniformly achieved. Moreover, immediately after occlusion of the brachiocephalic and subclavian arteries a dramatic sustained systemic hypertension occurred in both normothermic and hypothermic animals, a result of carotid sinus and central vasomotor pressor reflexes.[10] This hypertension may well have been a factor in forcing blood from the lower intercostal and lumbar arteries to the anterior spinal artery and thence to the brain.

The survival results and subsequent studies of the brains in the surviving dogs in this group demonstrate a definite threefold increase in cerebral arterial occlusion time tolerated by the hypothermic animals as compared with the normothermic ones. Because the arterial occlusion was not uniformly absolute, however, confirmation of the studies of Rosomoff and Holaday [2] must await a better method.

Kabat and Dennis,[7] in 1938, described the first method of producing cerebral ischemia to yield uniform results. This laminectomy and pneumatic-cuff technique was used extensively by them in normothermic dogs to study behavior patterns and reflex changes after specific periods of total ischemia.[9] A detailed microscopic study of the acute brain changes utilizing this technique was reported by Grenell.[11] The same six- to eight-minute survival range for the normothermic animals after occlusion by this method which these authors report was found in the present study. It is remarkable that animals survive occlusion only half as long by this technique as do dogs in Group 3 in which the aorta and venae cavae are clamped. Spinal cord compression is an integral part of the cuff method. This additional injury may have accounted for the difference in the occlusion periods tolerated by the two groups. Clipping of the basilar artery, instead of a preliminary laminectomy, to avoid spinal cord compression with the pneumatic cuff, has been utilized by Pontius and co-workers.[12]

The method employed to produce arterial and venous occlusion at the heart was based on the principle of "the azygos factor," as described by Andreasen and Watson.[13] Inflow to the right heart was entirely occluded, except for that coming from the azygos vein. The pulmonary circuit was left open and the aorta clamped just distal to the coronary ostia. With this preparation, the hearts remaining well oxygenated and continuing at a regular rhythm, occlusions were permitted both during normothermia and during hypothermia well beyond the time period which resulted in lethal brain damage. On release of the clamps, no change in rhythm occurred. The final end-point for the heart under these conditions was not determined.

In grading the extent of damage to each brain studied (Table 4), attention was focused primarily on the cerebral and cerebellar cortex. These areas have been repeatedly demonstrated to be most sensitive

to anoxia.‡ Acute changes in the cells of the upper lamina of the cerebral cortex, such as blanching, ghost-cell formation, pyknosis, and areas of "fall-out," were looked for and evaluated. The late changes were those of gliosis. The Purkinje cells and granular layer of the cerebellar cortex were carefully inspected for signs of injury. Permanent late lesions in these areas were the criteria used to define significant pathologic damage, and a rough grading system was employed.

Grossly, all the brains in the surviving dogs appeared normal. One control dog was killed two weeks after undergoing hypothermia alone; in this dog cooling per se produced no histologic evidence of brain injury.

The third method used in this study (arterial and venous occlusion at the heart) is of particular interest in that it simulates closely the effect of circulatory arrest as far as the brain is concerned. The accepted "critical" period of ischemia to the human brain under normothermic conditions is three to five minutes. Neubuerger[14] has recently reviewed the reported cases of circulatory arrest in which brain studies were made. Considerable variability was encountered, with severe changes seen after an arrest of only one minute; yet one case after an arrest of six minutes showed no residual changes. Complete arrest of 10 minutes, however, seemed always to lead to irreversible changes. The normothermic dogs in Group 3 demonstrated significant pathologic changes between four and eight minutes, a time period roughly comparable with that in the human cases reported. Hypothermia to 25 C prolonged the "safe" period to 12 minutes. This may well represent the upper limit of safety for open-heart procedures during hypothermia as currently applied.

TABLE 4.—*Summary of Estimated Brain Damage with Occlusion Times in Surviving Dogs*

Group 1: Arterial Occlusion Alone

Normothermia			Hypothermia		
Occlusion Time, Min.	Survival Time	Damage	Occlusion Time, Min.	Survival Time	Damage
6	2 wk.	0	10	3 mo.	0
10	2½ mo.	+	20	3 mo.	0
14	2 wk.	++++	30	4 days	+
			45	3 mo.	++++

Group 2: Arterial and Venous Occlusion at the Neck

Normothermia			Hypothermia		
Occlusion Time, Min.	Survival Time	Damage	Occlusion Time, Min.	Survival Time	Damage
2	3 mo.	0	6	3 mo.	0
4	2½ mo.	0	8	2 wk.	0
6	2 wk.	+++	8	2½ mo.	0
			10	9 days	0
			12	2 wk.	+++
			12	3 mo.	++

Group 3: Arterial and Venous Occlusion at the Heart

Normothermia			Hypothermia		
Occlusion Time, Min.	Survival Time	Damage	Occlusion Time, Min.	Survival Time	Damage
2	3 mo.	0	4	3 mo.	0
4	3 mo.	0	12	11 days	0
8	2½ mo.	++	14	5 days	+++
10	2 wk.	+++	14	2 mo.	++
10	3 mo.	++	16	5 days	++++
12	8 days	++++	22	2 mo.	++++

SUMMARY

Three methods were used for the production of temporary circulatory ischemia to the brain of the dog: one by occluding the arterial supply alone and two by occluding the arterial and venous circulation simultaneously.

Hypothermia of 23-26 C produced a threefold increase in occlusion time based on survival and comparable brain changes when the arterial supply alone was occluded, and a twofold increase with simultaneous occlusion of the arterial and venous circulation.

Correlation of these findings with their practical application in open-heart surgery and cardiac arrest is discussed.

The pathologic evaluation of the brain sections was performed by Dr. Karl T. Neubuerger. The general statements in this report will be detailed and documented in a forthcoming report by Dr. Neubuerger.

‡ References 14-17.

DISCUSSION

DR. DENTON A. COOLEY, Houston, Texas: I should like to comment on Dr. Marshall's excellent paper. Dr. Pontius, working in our laboratory, has done similar experiments, and the results were reported at the Forum Session of the American College of Surgeons last year. The experiments were undertaken on the assumption that complete occlusion of the cerebral circulation in the dog would be a rather simple problem. However, it was not until more than 30 dogs had been utilized that a satisfactory technique was worked out. The method that Dr. Pontius finally used was to approach the basilar artery inside the skull through the cerebrum magnum and occlude it with a clip. The carotid and vertebral arteries were occluded bilaterally. A cuff was then placed around the neck of the dog and inflated to 900 mm. Hg for 30 minutes. By these maneuvers ischemic changes were produced in only 66% of the animals; thus, the dog does not appear to be a very good experimental animal for this purpose. Nevertheless, Dr. Pontius concluded that hypothermia has the same protective influence upon cerebral tissues that it has upon the spinal cord tissue under these circumstances.

DR. J. CUTHBERT OWENS, Denver: I should like to report a clinical application of cerebral arterial occlusion during hypothermia. To date, we have attempted to use it on two neurosurgical patients. However, on one patient, after cerebral inflow was approached for occlusion in the neck, the lesion at the base of the brain was found to be inoperable, and actual occlusion was not undertaken. Occlusion in the second patient was for two periods of three and one-half minutes and four minutes, respectively. This patient had an aneurysm of the internal carotid artery which had ruptured one week before operation. Our approach was to occlude the subclavian arteries on either side of the vertebrals and both common carotid arteries. No attempt was made to occlude the vertebral arteries directly, in view of a previous report by Dr. James White, of Boston, of a case of thrombosis of the vertebral artery on the fourth postoperative day, after temporary occlusion of the cerebral circulation during hypothermia. The occlusion period allowed Dr. Keasley Welch, the neurosurgeon, time enough to have a dry field and place a clip at the base of the aneurysm without occluding the cerebral artery. The patient recovered from the operative procedure only to die two weeks later of extensive peritonitis caused by a ruptured ulcer of the cecum.

We are not satisfied with this method of approach for occlusion. Not only is it difficult to obtain direct vision during the occlusion time, since the neurosurgeon's field limits the space in which we are able to operate, but in addition six occlusion tapes or clamps are necessary in the field.

DR. ROBERT GOETZ, Capetown: My acquaintance with hypothermia is very short, but I should like to draw attention to a simple method of hypothermia which has been developed in Capetown and which perhaps some of you might like to use. A double-lumen tube is introduced into the stomach, the two ends of which are separated by about 4 in. A latex balloon is tied over the two ends through which cold water of 4 C to 10 C is being circulated. The balloon containing the cold water is in contact with the vascular stomach wall which is thus being cooled. This method is very simple and very efficacious in bringing the body temperature down.

DR. STROTHER B. MARSHALL, Denver: I want to thank Dr. Cooley and should like to point out that the work which was done on cerebral circulatory occlusion was only to determine what could be accomplished by hypothermia so far as the brain was concerned.

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Aortoiliac Stenosis

Diagnostic Significance of Vascular Hemodynamics

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Segmental obliterative disease of the terminal aorta and iliac arteries has recently received increasing attention. A great number of reports * have shown that its underlying pathologic process is atherosclerosis leading progressively to thrombus formation, that the lesions may begin at the bifurcation or most frequently in one or both common iliac arteries (Fig. 1), and that the development of these lesions is slow, insidious, and progressive.

From the clinicopathologic standpoint it may be emphasized that this syndrome may go through two distinct phases: stenotic and occlusive. Recent experience † with aortic resection and graft replacement in the treatment of the aortoiliac syndrome appears to indicate that when surgery is performed at an early stage the results are much more gratifying. Therefore, detection of this arterial disease at its stenotic stage may prove of practical value.

In a previous experimental work on stenosing arterial thrombosis,[10] it was shown that while a reduction up to 60% of the diameter of the aorta induced insignificant blood pressure changes, a reduction of the lumen between 60% and 70% resulted in significant manometric changes. When the stenosis reduced the diameter by 70%, a critical stage was reached beyond which any further decrease of the lumen caused sharp reduction in the mean pressure, thereby creating a hemodynamic state leading to a severe degree of arterial insufficiency. The present study in man was undertaken in order to gain some insight into the arterial hemodynamics at the stenotic phase of the aortoiliac syndrome in the hope that these hemodynamic findings may be of help in detecting the disease at its precritical or critical stage.

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From the Surgical Division, Peripheral Vascular Service, and the Medical Division, Montefiore Hospital.

Presented at the Third Scientific Meeting of the North American Chapter of the International Society of Angiology, Atlantic City, N. J., June 4, 1955.

* References 1-8.

‡ References 8 and 9.

CLINICAL DATA

This investigation is based on a correlative study of the clinical, roentgenologic, and intra-arterial pressure findings in 13 patients with the aoroiliac syndrome. Ten patients were men, and three were women, and their ages ranged from 37 to 75, with an average age of 57.5 years. A careful clinical history and objective circulatory findings in the lower extremities were recorded in each case. All patients exhibited clinical manifestations of arterial insufficiency. Usually a unilateral and in some cases bilateral "high" intermittent claudication, at the hip-gluteal-thigh level, was present, although occasionally predominant leg pain was also noted. Skin temperature, color changes, elevation-dependency test, trophic changes, arterial murmurs, arterial pulsations, and oscillometry were studied in each patient. Translumbar aortography was performed in 6 of the 13 cases. Intra-arterial pressure studies were done in all cases. Bilateral femoral tracings were taken in 11 cases, and unilateral femoral tracings, in 2. Palpation of the femoral arteries revealed slight to marked diminution of the pulse in 14 instances, its absence in 1, and "normal" pulse in 11. Systolic hypertension was present in 62% of the cases.

Murmurs were heard over the femoral artery in 15 instances and were recorded simultaneously with the ECG in 10. In most cases a loud systolic murmur could also be heard over the abdominal aorta, just above and lateral to the umbilicus. It is noteworthy that in the cases with marked diminution of

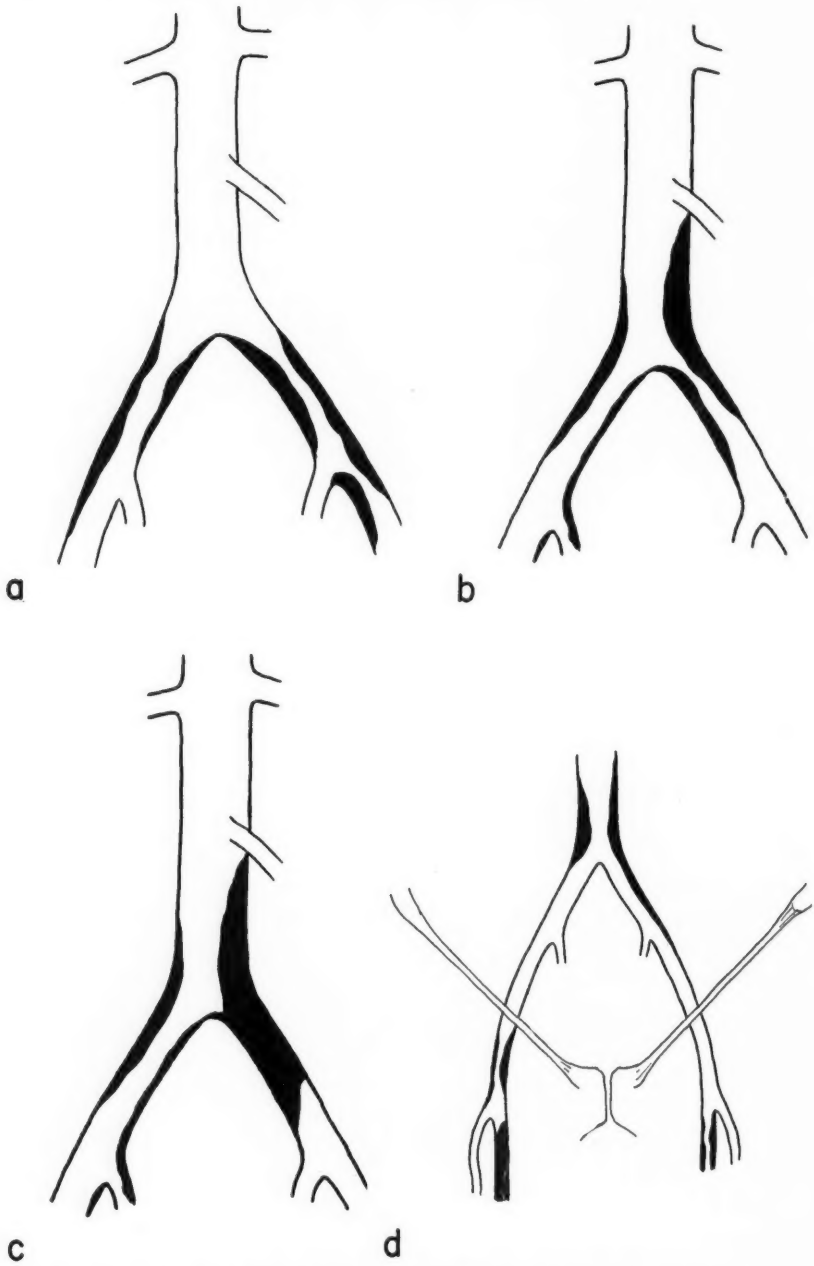


Fig. 1.—Drawings of the aortic bifurcation and iliac arteries showing various stages of incomplete occlusion: (*a*) stenosis of iliac arteries; (*b*) stenosis of the aortoiliac segment; (*c*) stenosis of the aortoiliac segment with complete occlusion of one iliac artery; (*d*) diffuse arterial pathology including aortoiliac stenosis and femoral occlusion and stenosis.

the pulse the murmur could not be heard. This clinical observation may be explained by the experimental findings of Gupta and Wiggers.[11] These authors, studying experimental aortic coarctation, have noted that the magnitude of the constriction is not strictly proportionate to the intensity of the murmur. A murmur occurred when 60% of the aortic lumen was occluded, reached its greatest intensity at 73%, and was no longer audible when the obstruction was more than 78%.

In addition to the group of 13 patients with the aortoiliac syndrome, 10 control subjects were also studied. Of these, seven had normal blood pressure and three had systolic hypertension, but none had any manifestations of peripheral vascular disease. Seven were males and three were females, and their ages ranged from 18 to 67, with an average of 52.3 years.

TABLE 1.—*Average Intra-Arterial Pressures in Control Subjects and in Patients with Aortoiliac Stenosis*

	Brachial Pressure, Mm. Hg*				Femoral Pressure, Mm.Hg*			
	Systolic	Diastolic	Mean	Pulse Pressure	Systolic	Diastolic	Mean	Pulse Pressure
Control	137 (109-178)	73 (55-92)	96 (75-124)	64 (44-90)	146 (115-200)	73 (55-96)	102 (80-135)	73 (48-111)
Stenosis, minimal	168 (129-226)	79 (63-115)	116 (84-158)	89 (64-117)	159 (117-226)	79 (64-116)	114 (85-169)	80 (53-110)
Stenosis, moderate	155 (122-226)	77 (52-115)	108 (80-158)	78 (64-111)	140 (112-207)	82 (60-121)	107 (85-170)	58 (46-86)
Stenosis, marked	172 (143-212)	77 (62-95)	114 (90-147)	95 (72-117)	113 (80-139)	76 (55-91)	97 (75-132)	37 (13-52)
Occlusion	137 (122-150)	70 (52-90)	97 (80-115)	67 (50-82)	56 (49-63)	48 (43-55)	53 (46-60)	8 (6-10)

* Figures in parentheses represent range of variation.

MANOMETRIC DATA

The intra-arterial pressures were recorded simultaneously from one brachial and both femoral arteries through Statham strain-gauge manometers connected to 18-gauge Cournand needles. Great care was exercised to avoid producing a hematoma when inserting the needle into the artery. The simultaneous records included the systolic, diastolic, and mean pressures, as well as the ECG.

1. In the control group, the average femoral systolic and pulse pressures were both found to be higher than the corresponding brachial pressures (Table 1). This relationship held true in normotensive and hypertensive subjects. The average brachial systolic pressure was 137 mm. Hg, with a range of 109 mm. Hg to 178 mm. Hg. The average femoral systolic pressure was 146 mm. Hg, with a range of 115 mm. Hg to 200 mm. Hg. The brachial pulse pressures ranged from 44 mm. Hg to 90 mm. Hg, with an average of 64 mm. Hg, and the femoral pulse pressures ranged from 48 mm. Hg to 111 mm. Hg, with an average of 73 mm. Hg. The femoral to brachial pulse pressure ratio (PP F/B) ranged from 1.03 to 1.27, with an average of 1.14 (Table 2). Tracings of arterial pressures obtained from control subjects exhibited normal characteristics (Fig. 2).

2. In the subjects with the aortoiliac syndrome, the manometric findings varied with the degree of arterial stenosis (Table 2). In contrast to the control group, the average femoral systolic and pulse pressures were found to be lower than the corresponding brachial pressures. The most striking manometric alteration resulting from any degree of arterial obstruction was reflected in changes of the pulse pressure, especially in its femoral to brachial ratio. Using this ratio (PP F/B) as a criterion, the hemodynamic findings can be classified in four patterns (Table 2): minimal stenosis, moderate stenosis, marked stenosis, and complete occlusion.

(*a*) Minimal stenosis was noted in nine instances. The average of both femoral systolic and pulse pressures were, respectively, 10 mm. Hg and 9 mm. Hg lower than the corresponding brachial pressures. The average PP F/B ratio was 0.90, with a range from 0.81 to 0.99.

(*b*) Moderate stenosis was noted in six instances. The averages of both femoral systolic and pulse pressures were, respectively, 15 mm. Hg and 20 mm. Hg lower than the

TABLE 2.—*Femoral to Brachial Pulse Pressure Ratio (PP F/B)*

	Cases, No.	PP F/B	
		Range	Average
Control	10	1.03-1.27	1.14
Stenosis, minimal	9	0.81-0.99	0.90
Stenosis, moderate	6	0.67-0.79	0.74
Stenosis, marked	7	0.18-0.48	0.39
Occlusion	3	0.06-0.16	0.12

corresponding brachial pressures. The average PP F/B ratio was 0.74 and the range from 0.67 to 0.79.

The aortogram shown in Figure 3 best illustrates the correlation between the angiographic and manometric findings of the preceding two stenotic patterns. This aortogram is that of a 49-year-old man whose chief complaint was bilateral hip claudication of more than one year's duration, with this symptom complex more pronounced on the left side. There is a filling defect at the aortic bifurcation and at the origin of both iliac arteries. The degree of stenosis is more pronounced on the left side of the aorta and the corresponding iliac artery. Figure 4 shows the manometric findings in this patient. From the angiographic and manometric findings it appears that there is a minimal stenosis on the right side and a moderate stenosis on the left.

(*c*) Marked stenosis was noted in seven instances. The averages of both femoral sys-

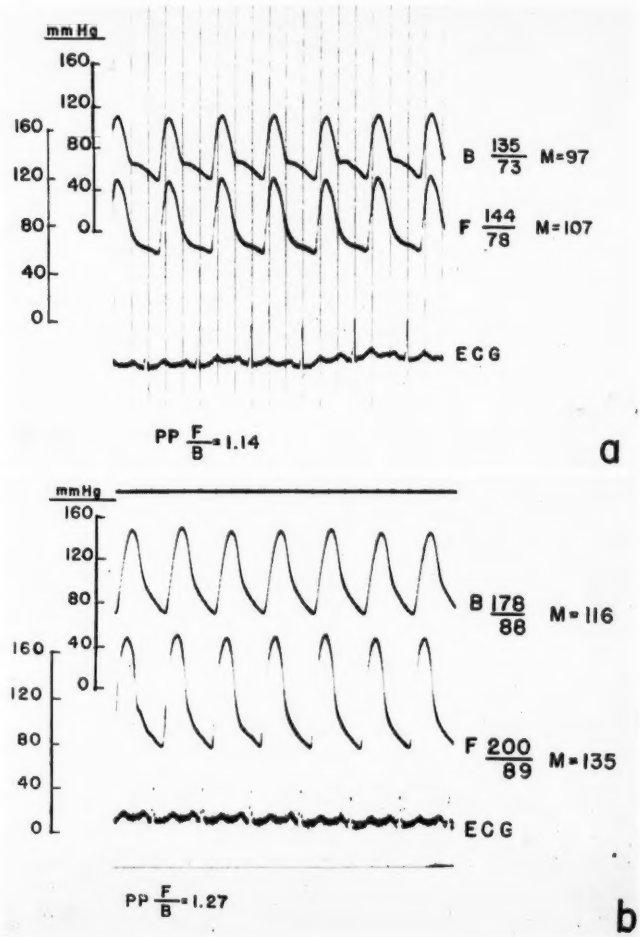


Fig. 2.—Tracings from intrabrachial (*B*) and intrafemoral (*F*) arterial pressures obtained from control subjects with (*a*) normal blood pressure and (*b*) arterial hypertension. PP F/B, ratio of femoral to brachial pulse pressure.

Fig. 3.—Aortogram from a 49-year-old man with intermittent claudication of the hips, more marked on the left side. Note filling defects of the aorta and its bifurcation, showing a more marked stenosis of the origin of the left iliac as compared with the right (diagram in inset).

tolic and pulse pressures were, respectively, 59 mm. Hg and 58 mm. Hg lower than the corresponding brachial pressures. The PP F/B ratio averaged 0.39 and ranged from 0.18 to 0.48.

Figure 5*a* is the aortogram of a 66-year-old man whose chief complaint was severe intermittent claudication of the right hip and it shows a marked stenosis of the right common iliac artery. A close-up of this aortogram (Fig. 5*b*) reveals that the diameter of the right iliac artery, at the stenotic level, is reduced to about one-sixth of that of the proximal vessel. Figure 6 shows the manometric findings in this patient, with a right PP F/B of 0.18 and a left PP F/B of 0.82, indicating a marked stenosis of the right side and a minimal stenosis of the left. The angiogram is in close agreement with these findings.

Another illustration of this degree of stenosis is shown in Figure 7. The arterial tracings in this Figure were obtained from a 52-year-old man with bilateral hip intermittent claudication, more marked on the left. The manometric findings indicate a moderate stenosis on the right side and a marked stenosis on the left, with a characteristic "saw-toothed" contour of the latter arterial tracing.

(*d*) Complete occlusion was noted in three instances. As shown by the aortograms, complete occlusion involved one iliac artery in two cases and the terminal aorta with its bifurcation in the third case. Despite complete occlusion, a femoral pulse, although very diminished, could be felt on the affected sides.

The averages of both femoral systolic and pulse pressures were, respectively, 81 mm. Hg and 59 mm. Hg lower than the corresponding brachial pressures. The average

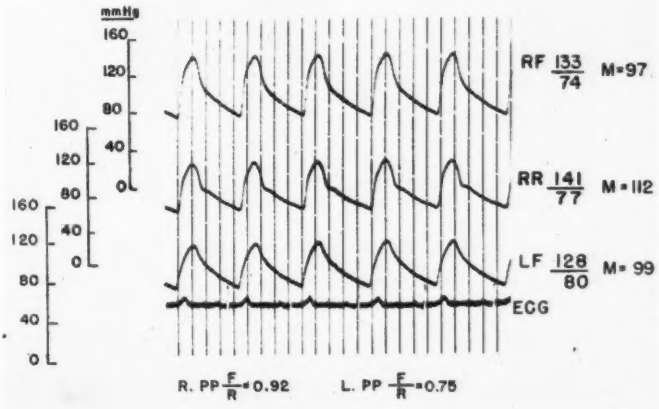


Fig. 4.—Tracings from intraradial and intrafemoral arterial pressure obtained from the patient whose aortogram is shown in Figure 3. Upper tracing, right femoral (mild stenosis); middle tracing, right radial; lower tracing, left femoral (moderate stenosis). PP F/B, ratio of femoral to brachial pulse pressure; M. mean.

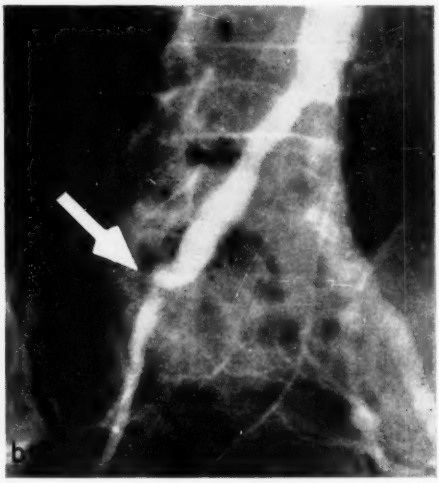


Fig. 5.—(*a*) Aortogram from a 66-year-old man with severe intermittent claudication of right hip. Note marked stenosis of right common iliac artery. (*b*) Close-up of the stenotic segment.

PP F/B ratio was 0.12, with a range from 0.06 to 0.16.

Figures 8, 9, and 10 illustrate these cases. Figure 8 is the aortogram of a 65-year-old man whose chief complaint was intermittent claudication of the left hip, and it shows complete occlusion of the left iliac artery. A faint femoral pulse was felt and was recorded as shown in Figure 9. The manometric findings in this patient indicate on the right side a moderate stenosis, with a PP F/B ratio of 0.77, and on the left side an occlusion, with a PP F/B ratio of 0.06.

Figure 10 is the aortogram of a 44-year-old man, showing a complete occlusion of the lower abdominal aorta and its bifurcation. A faint femoral pulsation was revealed through a cut-down in the right groin, with

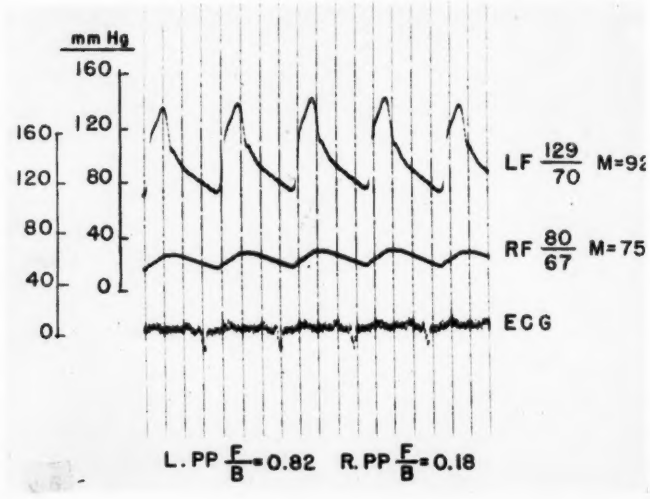


Fig. 6.—Tracings from intrafemoral arterial pressures obtained from the patient whose aortogram is shown in Figure 5. Upper tracing, left femoral (mild stenosis); lower tracing, right femoral (marked stenosis). Note the rounded arterial wave of the latter. PP F/B, ratio of femoral to brachial pulse pressure; M, mean.

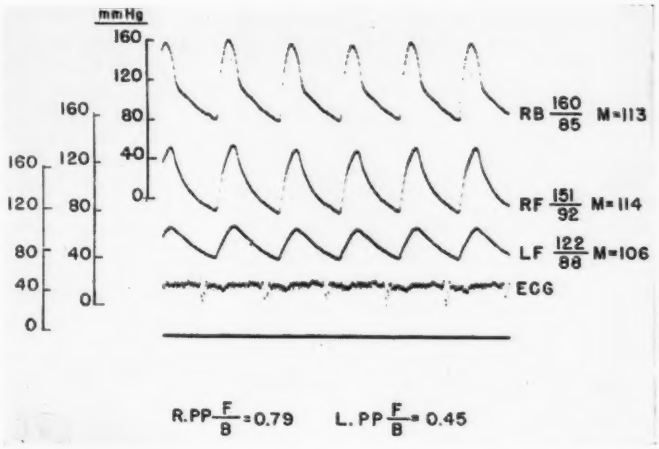


Fig. 7.—Tracings from intrabrachial and intrafemoral arterial pressures obtained from a 52-year-old man with bilateral hip intermittent claudication, more marked on the left. Upper tracing, right brachial; middle tracing, right femoral (moderate stenosis); lower tracing, left femoral (marked stenosis). Note the "saw-toothed" contour of the latter tracing. PP F/B, ratio of femoral to brachial pulse pressure.

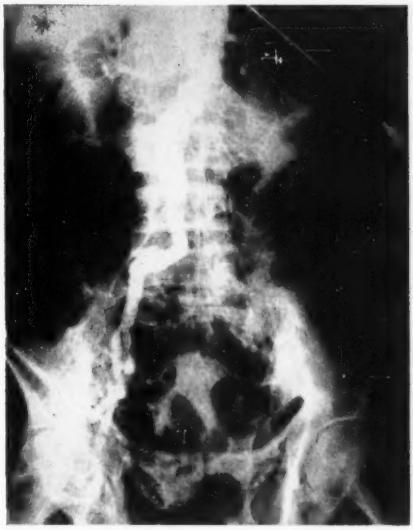
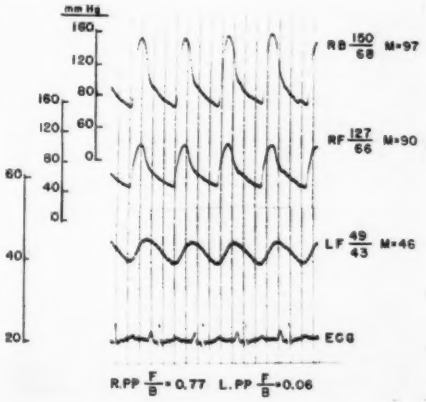


Fig. 8.—Aortogram of a 65-year-old man with left hip intermittent claudication. Note complete lack of visualization of the left iliac artery, although a faint femoral pulse was felt and recorded, as seen in Figure 9.

a blood pressure of 63/55 mm. Hg, a mean of 60 mm. Hg, and a PP F/B of 0.16. These hemodynamic findings ilustrate the pattern of minimal pulsatile flow in a femoral artery via collateral branches below the extensive aortoiliac obstruction.

Analysis of the femoral arterial pressure tracings in the aortoiliac syndrome shows the following characteristic features: (1) The pulse wave rises slowly; (2) its amplitude is reduced; (3) in minimal and moderate stenosis the peak is rounded and the dicrotic limb descends slowly; (4) in marked stenosis the pulse curve consists of a rounded wave with a shallow dicrotic notch, having often a "saw-toothed" contour; (5) in complete occlusion it usually consists of a simple rounded wave; (6) the onset of the femoral pulse wave and the interval of time elapsing between the onset and the peak of this wave

Fig. 9.—Tracings from intrabrachial and intrafemoral arterial pressures obtained from the patient whose aortogram is shown in Figure 8. Upper tracing, right brachial; middle tracing, right femoral (moderate stenosis); lower tracing, left femoral (occlusion). The lower tracing was recorded with a higher amplification than the upper ones. Note its rounded wave contour. PP F/B, ratio of femoral to brachial pulse pressure.



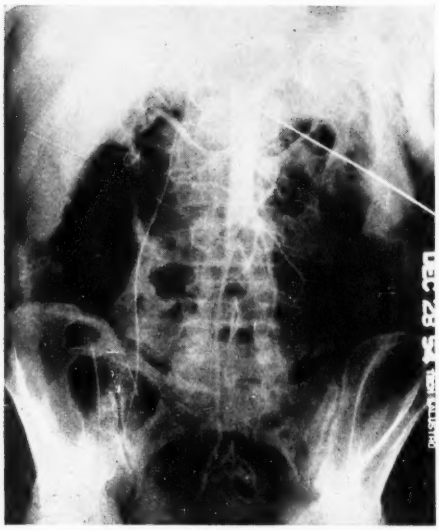


Fig. 10.—Aortogram of a 44-year-old man, showcomplete occlusion of the lower abdominal aorta just below the inferior mesenteric artery. For manometric findings recorded from the femoral artery, see text.

are delayed as compared with the normal waves. Table 3 indicates that the onset to peak of the femoral pulse exhibits an average delay of 0.04 second, 0.08 second, and 0.10 second in cases of moderate stenosis, marked stenosis, and complete occlusion, respectively, as compared with the control group. The latter findings are essentially in agreement with those reported by Brown and coworkers [12] in their study of intra-arterial blood pressure in patients with coarctation of the aorta.

TABLE 3.—*Average Arterial Pulse Propagation Time*

	Delay in Onset of Femoral Pulse Wave, Sec.*	Onset to Peak of Femoral Pulse Wave, Sec.
Control	0.00 (−0.04-+0.01)	0.15 (0.10-0.21)
Stenosis, minimal	0.00 (−0.02-+0.01)	0.15 (0.10-0.22)
Stenosis, moderate	0.00 (−0.01-0.00)	0.19 (0.13-0.25)
Stenosis, marked	−0.01 (−0.03-0.00)	0.23 (0.19-0.28)
Occlusion	−0.03 (−0.08-0.00)	0.25 (0.20-0.33)

* Difference between onset of femoral pulse wave and brachial pulse wave.
Figures in parentheses represent range of variation.

ACUTE GRADUATED AORTIC STENOSIS

In order to assess more fully the quantitative relationship between the degree of stenosis and the corresponding hemodynamic alterations, a series of acute graduated stenosing experiments was performed in the dog. A number of tubes of known diameter, ranging from 0.8 mm. to 4.9 mm., were introduced into the abdominal aorta, between the renal arteries and the aortic trifurcation, and the intra-arterial pressures in the femoral and brachial arteries were recorded simultaneously. The details of this experimental work will be reported elsewhere.

Manometric results of a representative experiment are shown in Figure 11. It illustrates the relation between the degree of aortic stenosis and the femoral pressure reduc-

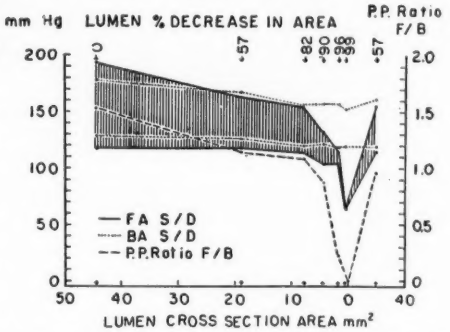


Fig. 11.—Relation between the degree of acute gradual aortic stenosis and femoral artery pressure reductions. Note the existence of a critical stenosing point occurring at 82% of cross-section area reduction of the lumen. Also note that the PP F/B ratio exhibits greater reductions than the other manometric changes after the critical point is reached.

tions. From this diagram it can be seen that the brachial systolic and diastolic pressures remain relatively unaltered during the entire experiment, while the femoral systolic and diastolic pressures exhibit a sharp fall at a point corresponding to a reduction of 82% in the cross section area of the aortic lumen, which thus represents the critical stenosing point. The control PP F/B ratio was 1.54. When the cross-sectoin area reduction reached the critical stenosing level, this ratio was 0.76. Beyond this point both the blood pressures and the PP F/B ratio exhibit sharp reductions. These findings corroborate

the hemodynamic findings in the aortoiliac stenosis in man.

COMMENT

The clinical manifestations associated with the aortoiliac syndrome may vary with the degree of arterial obliteration. Since Leriche's classic description of the complete thrombotic occlusion of the terminal aorta,‡ most reports on this subject have failed to make the distinction between stenosis and occlusion. As a result, many clinical reports have been at variance with Leriche's original description.

While in the majority of the cases with complete obliteration there is absence of peripheral pulses, marked intermittent claudication, muscular atrophy, and impotence, in the cases with stenosis, peripheral pulses, although diminished, may be felt and all the other manifestations may be absent or less marked.

It is likely that the stenosis is only an early stage of this process leading ultimately to complete aortoiliac occlusion. Unlike the latter stage, which is easily recognized, the diagnosis of aortoiliac stenosis may be difficult and indeed is often missed. Its recognition, however, may prove of value from a therapeutic standpoint, especially in cases of segmental lesions.

The findings of the present investigation indicate that direct intra-arterial measurements of the pressures may help in the diagnosis of stenosis and may also afford a quantitative estimation of its degree. They also suggest that stenosis of the terminal aorta and iliac arteries may be present for long periods in a subclinical state until it reaches a certain degree which will result in perceptible to pronounced hemodynamic changes.

In a previous work [10] acute graduated aortic stenosing experiments in the dog have shown that a reduction of the diameter of the lumen up to 60% induces insignificant blood pressure changes. In the present investigation similar results were obtained when the cross-section area of the lumen was reduced up to 82%. In both sets of experiments a critical point was shown to exist: in the former at about 70% of diameter reduction and in the latter at about 82% of cross-section area reduction.

Observations reported by others [13] in a study correlating blood flow changes with the decrease of the lumen of the carotid artery in the dog are in close agreement with our findings. Likewise, Wylie and McGuinness,[14] reporting on arteriosclerotic stenosis of the aorta and iliac arteries in man, have presented data suggesting that the lumen of a major artery must be reduced by about 90% to produce impairment of blood flow sufficient to cause ischemic symptoms distal to the level of stenosis.

While the arterial pressure reductions may not be significant before the critical point is reached, the contour of the arterial waves and the PP F/B ratio already reveal hemodynamic alterations. Slow rise of the pulse wave, reduced amplitude, rounded peak, slow descent of the dicrotic limb, shallow dicrotic notch, and a PP F/B ratio below 1.00 appear characteristic of the precritical stage of the arterial disease.

After the critical point has been reached, alterations of the arterial waves become pronounced. A "saw-toothed" contour or a rounded wave, a lag in the propagation time of the femoral pulse as compared with that of the brachial, and a significant delay of the time elapsed between the onset to the peak of the femoral wave are characteristic changes of marked stenosis or near-complete occlusion of the lumen.

The correlation of the clinical and angiographic data with the PP F/B ratio suggests the latter to be a valuable index in the evaluation of the degree of stenosis. While in the control group the average PP F/B ratio was 1.14, with a range from 1.03 to 1.27, in the group with aortoiliac stenosis this ratio was always below 1.00. Indeed, when the clinical manifestations and the aortograms suggested only a minimal or moderate stenosis, the PP F/B ratio ranged from 0.67 to 0.99, with an average of 0.90 for minimal stenosis and 0.74 for moderate stenosis. Interpreted in

‡ References 1-3.

terms of percentage of cross-section area reduction, it appears that these ratios indicate a degree of stenosis ranging from about 57% to about 82%.

The apparent discrepancy between the actual degree of stenosis as shown by the cross-section area reduction and the "minimal" or "moderate" manometric and angiographic changes is in agreement with a previous work,[10] in which it was shown that the pathologic findings in arterial stenosis are more striking than the clinical and angiographic data would indicate. The terms "minimal" and "moderate" used in our classification apply thus to the degree of clinical and angiographic findings and not to the degree of vascular pathology.

In the cases of marked stenosis the PP F/B ratio ranged from 0.18 to 0.48, with an average of 0.39. In complete occlusion it ranged from 0.06 to 0.16, with an average of 0.12. Interpreted in terms of cross-section area reduction, the PP F/B ratios in marked stenosis indicate a degree of narrowing of the lumen ranging from 82% to 99%, i. e., near-complete occlusion. It is interesting to note that the manifestations of marked stenosis occur at or beyond the critical stenosing point.

It should be pointed out that a segmental occlusion with a well-developed collateral circulation may exhibit hemodynamic alterations similar to those of marked stenosis. In this case, an aortogram may help in differentiating the two conditions. The patient whose aortogram is shown in Figure 8 illustrates this point.

SUMMARY

Stenosis of the terminal aorta and iliac arteries may be present for long periods in a subclinical state until it reaches a certain degree which will result in perceptible to pronounced hemodynamic changes.

A critical point of about 70% reduction in diameter or 82% reduction in cross-section area of the lumen is necessary before significant manifestations of blood flow impairment are present.

The most striking hemodynamic alteration associated with arterial stenosis is reflected in changes of the pulse pressure, especially in its femoral to brachial ratio (PP F/B). Using this ratio as a criterion, the arterial disease may be classified as minimal stenosis, moderate stenosis, marked stenosis, or complete occlusion.

In minimal to moderate stenosis the aortogram shows insignificant filling defects, while the arterial pressure tracings indicate characteristic changes.

In marked stenosis the aortogram indicates narrowing of the lumen and the arterial pressure curves exhibit a characteristic "saw-toothed" contour or a rounded wave.

A segmental occlusion with a well-developed collateral circulation may exhibit hemodynamic changes similar to those of a very marked stenosis. An aortogram may help in differentiating the two conditions.

The degree of stenosis induced by the thrombus is always more pronounced than the clinical and angiographic findings would indicate.

The PP F/B ratio appears to be an index of the degree of stenosis. Its diagnostic value is discussed.

Mr. William T. Nolan, Mr. Ruthven Ferreira, and Mr. Alphonso Henry gave technical assistance.

DISCUSSION

DR. ALTON OCHSNER, JR., New Orleans: I would like to ask Dr. Haimovici if he performed any experiments in which he altered the resistance distal to the point of pressure measurement in addition to altering it proximally. A change in distal resistance might be expected to change the diastolic and pulse pressures and thus affect the entire PP F/B ratio.

DR. GEZA DE TAKATS, Chicago: There is one question I would like to ask Dr. Haimovici. This is obviously a very important problem, but how does he feel about the ordinary oscillometer, which of course we know swings with various intensities and various heights before and after a given amount of muscular exercise and which would give him an idea of a critical iliac stenosis. I don't know whether I am making the question clear or not, but years ago, as you know, some of our members—perhaps Norman Freeman is here—talked about angiospastic claudication in the type of patient who would lose his pulse or whose oscillometric curve would get flatter after exercise. Many of these patients obviously have stenosis, and this is simply an expression of a lack of sufficient circulation dur-

ing stress, which brings up the problem of whether or not these finer earlier stenoses could not be recognized after graded amount of exercise in a limited area.

DR. TRAVIS WINSOR, Los Angeles: We have been very much interested in this problem from a purely indirect point of view and have by means of an appropriate recorder of an oscillometer type recorded similar changes of a delayed press time decreased amplitude and set up limits of ratios very similar, and it is amazing to me to see the similarity in pulse form which is obtained by the direct method of Haimovici and the indirect method, which of course has the disadvantages of having fat, muscle, and skin, etc., between the recording cuff and the blood vessel itself. The point I would like to make is this: in the presence of disease of the arm I presume the index may still be quite normal if one had disease of both and, also, if one had disease of the arm and not of the leg the index would be of a reverse order and usually high. The point, of course, is quite obvious. I think that this information is of particular value in that it lends weight to the indirect method, which can be applied so easily in all persons. I also would like to make one comment regarding the vasomotor tone of large vessels as Dr. de Takats brought up. We have seen, very definitely, changes in amplitude with various sympatholytic drugs and with heat, eliminating other factors that we thought were due to changes in the vasomotor tone of the larger vessels.

DR. HENRY HAIMOVICI, New York: In answer to Dr. Ochsner's question, I would like to state that in the course of this investigation we did not alter the peripheral resistance. What we actually measured was a proximal—an aortoiliac—hemodynamic change. I do not think that a reduction of the distal peripheral resistance could have appreciably influenced the arterial curves that we have obtained. With regard to Dr. de Takats' question on the use of the oscillometer in the study of arterial stenosis, I would like to say again that oscillometry was done in all cases. In the cases with mild to moderate aortoiliac stenosis the oscillometric readings at rest were usually diminished, while in the cases with marked stenosis the oscillometric readings were always much reduced. While exercise usually further diminished the oscillometric readings, the latter findings were not helpful in indicating the degree of stenosis at the aortoiliac level. With regard to the indirect method mentioned by Dr. Winsor, I would like to say that we have attempted to record the femoral pulses by the use of a glycerol pelote ("pulsometer") applied over the femoral arteries in the groin. The results obtained were very erratic. At best, the records showed only qualitative changes of the arterial curves but did not afford any quantitative estimation of the hemodynamic alterations involved.

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Correlation of Angiography with Surgical Treatment of Vascular Diseases

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The subject matter I present today overlaps to some extent that discussed by other speakers. Medicine and surgery, however, constantly overlap, especially in such specialties as vascular diseases. Discussion of these subjects from different viewpoints in many ways is good, because it permits various thought slants on the matter presented. My study of the use of angiography may be somewhat primary for this group. The number of patients, however, who arrive in our Clinic misdiagnosed indicates that one of the most important modalities for the interpretation of cardiovascular disease has not been utilized as much as it should be. This paper's purpose is to stress the importance of angiography, particularly before one elects and selects surgical intervention as the treatment of choice. I shall discuss, therefore, various lesions of the vascular system from a diagnostic and prognostic standpoint, their delineation by angiography, and the use of this method in the selection of the treatment of choice.

I. ARTERIOGRAPHY

The first subject for discussion is the use of angiography in the determination of the type of therapy in lesions of the arterial system. Nature has been provident in its supply of blood vessels to carry the circulation to many parts. In many of the organs, however, and, of most importance, in the end-vessels she has been negligent. Examples are the coronary system, the renal system, and the lower extremities. In a normal aortogram one can see how little collateral supply is available in an acute closure in contrast to that which will develop if a very slow occlusion occurs. The collateral supply develops in inverse proportion to the rate of occlusion. This means that in the acute occlusions there is very slight possibility of the collateral supply carrying the blood distally in many areas of the body. In a normal femoral arteriogram again one sees that even at the knee joint, where there are many articular branches, the vessels in most instances are not of sufficient size to carry on the circulation if the main artery occludes. Therefore, sudden occlusion in the popliteal artery is nearly always followed by gangrene.

My colleagues and I have studied the collateral circulation and differentiate it into three types.

1. *Hypervascularization.* — The hypervascularization type shows the minute vessels which either were preformed or were developed as a result of the occlusion. It is obvious that such vessels, while they may maintain vitality to the skin and other tissues, cannot supply enough blood to carry on the normal activity of the part. Thus, patients with only the hypervascularization type of collaterals can have no direct arterial replacement because there is no adequate distal artery available for grafting. This is important and appears obvious, but some surgeons have tried to graft without an open patent artery distally.

We believe in the routine medical measures for all such patients, including good hygiene,

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care of infections, complete abstinence from tobacco, administration of anticoagulants, and the use of the limb below the fatigue stage.

In our experience surgical sympathectomy has prevented gangrene in many patients with the hypervascularization type of collaterals, if it is done completely enough. We believe that the operation reduces the peripheral resistance in the arteriolar bed. The systolic pressure of blood as it leaves the heart is approximately 120 mm. Hg in the average person. By the time the circulation has reached the end-arteries, systolic pressure is approximately 90 mm. Hg, a loss of about a quarter of the propulsion force exerted by the heart. In the arteriolar bed the systolic pressure has dropped to 30 mm., and, therefore, a full one-half of the propulsion force of the heart has been expended in the arteriolar bed. A total of 94% of the blood is always en route to or from the capillaries, and only 6% is in the capillaries. It takes two and a half times the pressure to go through the arteriolar bed as it does to go from the heart to the end-arteries. The internal resistance in an arteriole is 1000 times greater than that in a terminal artery branch. A reduction in the resistance in this arteriolar bed, which we believe occurs after sympathectomy, well explains the fact that there is clinical improvement in many of these patients and that the force as it is exerted finally on the capillary bed is adequate to carry on the tissue-cell-capillary exchange in this bed without the loss due to increased peripheral resistance. This peripheral resistance drop, plus the relaxation of spasm, is our concept of the beneficial function of surgical sympathectomy in these patients. We expect soon to be able to prove this point.

2. *Supplemental Branches.*—The second type of collateral circulation is that of the supplemental branches. The vessels dilate, and the secondary vessels around the knee joint are examples. These are capable of enlarging and sometimes can carry the circulating load necessary for restricted physical activity.

3. *Bridging Collaterals.*—The third type we call bridging collaterals. Many of the patients are able to get along after an occlusion of a major vessel with minor circulatory deficiencies if the occlusion develops slowly for a long time; the reason is that some of the blood flow has been detoured from the major vessels to other collaterals of a supplementary type until they have become enlarged. Many, however, require circulatory help. Most of the patients with supplementary branches or bridging collaterals can expect to have a good result from a graft if there is a good circulatory channel beyond the block. If not, a bypass or graft will fail. All these patients also have a complete surgical denervation.

We have bypassed these occlusions by arteriotomy with thrombectomy, by analogous vein grafts, by homografts, and by prosthetics. In our experience the intimectomy method has been the least effective. These patients have also had surgical sympathectomy. We have also used analogous veins, inserting them by end-to-side fashion above and below the block to avoid injuring the collaterals.

The complete occlusion at the bifurcation of the aorta usually results in death. For this syndrome the homologous frozen dry grafts from the New York Vessel Bank are used. For the obstructions in the iliac artery nylon grafts have proved most effective. We are using ones which have corrugations. These crimps permit a banjo-like expansion of the graft with the heart impulse and do away with the objection to the prosthetic graft that it cannot expand with the heart beat.

In aneurysms a special problem is met. Many of the traumatic type can be repaired, and such a procedure is an ideal solution to the problem of an aneurysm fed by a tiny aperture in the artery. In the sclerotic type a homologous or nylon graft has been curative. For the large aortic aneurysms we use homologous grafts. The x-ray helps, however, and in some (of a nine months' pregnancy size) the wiring technique devised by Moore, Carrodi, and Blakemore combined with a mesh covering has ameliorated the symptoms and delayed the final outcome; in one such case, more than two years was added to the patient's life.

II. VENOGRAPHY, AFTER PHLEBITIS

A few years ago I made a statement which I have regretted many times. I said that it was difficult for us in our clinic to adequately interpret a venogram. I am certain that our difficulty was due to faulty venography technique and our own inability to interpret the picture. Since that time all our patients who have had a thrombosis or phlebitis of a deep or superficial type have a venogram performed before operation. The technique consists of the injection of a solution of 35% sodium acetrizoate (Urokon) sodium into the vein of the tourniqueted foot with the patient in a semirecumbent position. A tourniquet placed at the ankle forces the dye to go up the deep veins. X-rays are then taken at 40, 80, and 120 seconds, and at longer intervals if necessary, and the leak-backs from the deep to the superficial system are delineated and plotted. One can then operate on these patients, not by guess but by anatomic marking, and one can find the exact point at which one wishes to resect the incompetent vein. Many incompetencies in the peroneal system on the lateral aspect of the leg not diagnosable clinically have been found. Their resection has helped in the relief of the residual symptoms. The importance of venograms in our opinion is well illustrated by a venogram of one of our patients which shows a postphlebitic leg. A few years ago in such a patient we would have resected and stripped the superficial saphenous system. It is evident from this picture that while the deep veins are functioning below the knee, the only adequate venous return in this person from the knee to the groin is by the superficial saphenous system. The treatment, therefore, was to retain the saphenous system from the knee up and resect the incompetent points below the knee.

III. VENOGRAPHY, AFTER SUBCLAVIAN OR AXILLARY VENOUS THROMBOSIS

Another condition in which angiography is particularly important is in subclavian and axillary vein thrombosis. If one of four such patients, one could see the complete occlusion of the subclavian vein. Attention was drawn to the collateral circulation with the return of most of the blood by the jugular system. In a second patient there was an injury to the clavicle. Repeated efforts to obtain union of the clavicle had failed, and one could see a wire suture still *in situ*. Removal of the clavicle was not sufficient to prevent the repeated attacks of subclavian vein thrombosis. Scalenotomy was the surgical treatment for both of these persons. The scalenus anticus muscle arising from slips from all the cervical vertebrae and inserting on the first rib has the subclavian vein between it and the clavicle. In certain persons thrombosis of that vessel occurs spontaneously. In others, effort or posture causes the clot. Once such a thrombosis has taken place, recurrence of the clot is to be expected as long as the scalenus anticus muscle is present to cause vein pressure.

Three such patients have been referred to me with a diagnosis of "varicose veins of the upper extremities." In two of these patients these varicosities had been injected with sclerosing solutions, as one might do with simple varicosities of the lower extremities. The third patient had had repeated resections of these veins, which obviously were collateral veins and were necessary to the patient for the return of blood flow from the periphery of the arms.

IV. PORTAL PORTAGRAM AND SPLENIC PORTAGRAM

The fourth type of angiography of importance is the delineation of the portal system of veins and the splenic system prior to surgical therapy for hypersplenism, portal hypertension, and especially for esophageal varices, and hematemesis. This technique has been perfected by Drs. Rousselot and Ruzicka at St. Vincent's Hospital. The delineation is performed in two ways. A portagram can be made at the operation time as soon as the abdomen is opened. One of the vessels, such as an upper jejunal vein, can be canalized by a No. 15 polyethylene tube, pressure readings taken, and the dye (50 cc. of 50% sodium acetrizoate) injected. This will demonstrate at once the intra- and extrahepatic block,

whether the portal system is patent, and details regarding the collateral circulation already available. The splenic portagram is produced by a direct injection into the spleen through the chest wall at the ninth thoracic interspace. A dose of 50 cc. of 70% sodium acetrizoate is injected into the spleen when a free blood flow is obtained. This will demonstrate immediately the block area, and may avoid grave error in the selection of the incision site, as well as the type of shunt indicated for the relief of the portal hypertension or other definitive operations. If the proximal portal system is blocked, a portacaval shunt must fail. If a very large splenic vein is present, one could use that vessel for a shunt. If neither is present, an esophagogastrectomy or esophageal vein ligation and plication may be the treatment of choice. This type of angiography may be lifesaving in the individual patients.

I have illustrated many applied methods of using angiography. Again may I repeat that I believe we should use this modality not once in a while or occasionally but routinely in the diagnosis of difficult vascular problems, and particularly as a means of selecting the right surgical approach to the vascular problems presented.

DISCUSSION

DR. JERE W. LORD JR., New York: I have not felt quite so sanguine about contrast media studies in the determination of what to do for the patient. In a number of these conditions, however, once in a while these studies seem to be of great value in the care of the patient; of course, they are of great value in teaching. However, in view of the devastating military injuries in Korea and automobile accidents in this country, I would like to cite one case of what I thought was a traumatic aneurysm in which arteriograms were of real value. This man recently suffered a most extraordinary injury when a 20-lb. case of Wheaties fell on his lower thigh and caused a hematoma. He was operated upon shortly after his accident, eight years before I saw him; apparently the hematoma was drained. He was well until about eight years later, when he developed pain in his lower leg. He was seen by an orthopedic surgeon who diagnosed an aneurysm. The aneurysm, on examination, had a typical expansile pulsation and a systolic bruit which seemed to be located, not in the popliteal area, but a little more medially in the region of the muscle mass just above the patella near the vastus medialis. In view of the unusual location, we carried out an arteriogram at University Hospital, which illustrated instead of a false aneurysm as a result of trauma a cirsoid aneurysm coming off the superior medial geniculate branch of the upper popliteal or lower femoral artery. At operation I thought that I had removed all of this vascular mass, but not being completely satisfied, at the end of the procedure we postoperatively attempted an arteriogram. Since I was not able to do a percutaneous one, I abandoned the procedure and discharged him. There was no bruit or pulsation, and he seemed clinically well. He remained well for a year, at which time he noticed a little pain in the region of the excised aneurysm. On examination, there was a feeble pulse and a feeble bruit. The patient went to a clinic in the north for consultation, and an arteriogram was carried out which demonstrated that there had been either a persistence of the cirsoid aneurysm with enlargement as time went by or a recurrence. I think persistence was the better diagnosis. The patient came back to University Hospital, where we operated on him and removed, in this instance, the entire vastus medialis and intermedius muscles on the inner half from the midpatella up to the juncture of the lower and middle thirds of the thigh; this time the femur was exposed, and I believe that we completely removed the cirsoid aneurysm. A follow-up arteriogram was carried out about three weeks later, and I believe that now we have a cure. In this particular instance arteriography was valuable in the patient's care.

DR. EUGENE A. OSIUS, Detroit: For every pro there is a con and I think I would like to cite very briefly and quickly one of the things that happened with an aortogram that one of our residents did one morning. We are not against arteriography in any sense of the word, but I wonder how many of you have ever done an emergency abdominoperineal? By chance the needle got too close to the inferior mesenteric, and we had a most beautiful demonstration of the inferior mesenteric artery and its entire branches that I am sure could not have been repeated by careful dissection over six months' time. Twelve hours later this patient developed a very definite "acute belly." He was operated upon, and the entire distal portion of the descending colon and the rectum were necrotic. A colostomy had to be done. It is just an interesting incident, and I leave it to you for what it is worth.

Functional Venography as an Aid in the Study of Peripheral Venous Disorders

THOMAS C. MOORE, M.D., Muncie, Ind.

Peripheral venous disorders largely arise from the difficulties associated with the passage of venous blood from the dependent extremity toward the heart against gravity. Since venous return in the horizontal position presents no real problem, the crux of the matter lies in the adequacy of the mechanisms for combating the effect of gravity and providing for the continuous flow of blood from the dependent extremity. Muscle activity and tonus provide the principal force producing this flow. The direction of flow appears to be determined by the valves, the push of blood from the capillary bed, and the proximal emptying of blood from the venous reservoirs by passage through the right side of the heart and by the negative intrathoracic pressures produced by respiratory movements.

The assumption of an erect or semierect position through a sizable portion of each day imposes a substantial load on these relatively imperfect mechanisms for venous return and on the vascular bed as well. Since the margin of safety is not a wide one, any break in the chain of defenses against excessive pressure elevations, either from gravity or from muscle activity, may increase the likelihood of significant tissue damage and of further strain on the system. Although the pathologic changes directly responsible for the tissue alterations which may occur are not clearly understood, it does appear that such factors as elevated venous tension, venous stasis, and increased tissue fluid pressure and edema are involved.

The history and physical examination have been and remain the major avenues of study. It should be emphasized that ancillary measures such as venous pressure determinations and venography are still in the stage of clinical investigation. Although these measures may be of diagnostic assistance in selected cases, their principal value at present lies in their usefulness in advancing our knowledge of venous physiology and pathology. Their clinical employment must await further evaluation of the indications and the type of data which may be obtained and determination of whether such data may be secured by simpler means.

Although the origins of venography may be traced back to 1923, interest in its potential value in the study of venous function in the dependent extremity is of recent vintage. The importance of investigating venous return from the dependent extremity both in quiet dependency and with muscle activity has been stressed.[3]

It was my initial impression that percutaneous injection into the popliteal vein would prove to be the most useful.[4] However, increasing experience with injection into the superficial system has led to more frequent utilization of this route.[2]

The purpose of the present report is to describe the findings in 70 recent functional venographic investigations carried out both in normal control subjects and in patients with venous disorders of the lower extremi-

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ties. Injection into the superficial system, either percutaneously or through a cut-down polyethylene catheter, was performed in the majority of studies. Popliteal and femoral injections were employed only when additional information was desired. Thirty cubic centimeters of 30% sodium acetrizoate (Urokon sodium) was used in the majority of injections, and the x-ray table was uniformly tilted to an angle of 60 degrees, as in previous studies.

CONTROL STUDIES

No effort was made to obtain control observations with femoral or popliteal injections, because of previously reported investigations in which injection was made at these sites. This phase of the study, accordingly, concerns 17 functional venographic injections into the superficial system of persons who were judged to be free of lower extremity venous disorder on the basis of their histories and the physical findings. Although a few patients were studied by percutaneous injection into a vein on the dorsum of the foot, injection in the majority was carried out through a catheter which had been inserted by means of a cut-down at the level of the medial malleolus and threaded up to the middle of the calf. Percutaneous injection into the calf or thigh in control subjects was found to be difficult because of the scarcity of sufficiently large superficial veins in these areas.

When injection was made through a polyethylene tube, the tip of which generally was near the middle portion of the leg, the radiopaque material passed up the greater saphenous vein for varying distances and usually in decreasing concentration. The height of passage often varied with the speed of injection. Communicating veins were visualized at different levels, and the bulk of the injected material was seen to pass into the deep venous system and up it in the popliteal-femoral trunk against gravity in quiet, but weight-bearing, dependency. It is of interest that there was generally some distal regurgitation of the medium past several valve stations after it reached the deep system. This regurgitation occurred significantly beyond the lowest visible communicating channel. The material cleared from the deep system with exercise. Often tiny amounts of medium would remain behind in valve cusps, as was observed when injection was made directly into the deep system. The clearing of the medium with exercise was less complete from the superficial system than from the deep.

The venographic findings in two representative control subjects are illustrated in Figures 1 and 2. Similar functional superficial venograms were obtained in a patient with marked lymphedema in whom there was no evidence of venous disorder (Fig. 3). The patient had had a radical vulvectomy with bilateral radical groin dissection for squamous-cell carcinoma of the vulva approximately four months prior to the venographic study.

The tendency toward pooling of radiopaque medium in concentration in the foot and ankle areas, with considerable patient discomfort, led to the early, and perhaps premature, abandonment of percutaneous injection into the dorsum of the foot. There has been insufficient experience with injection into this area to comment on its possibilities.

ABNORMALITIES OF THE SUPERFICIAL SYSTEM

Both saphenous vein incompetency and superficial phlebitis were investigated. At times the two conditions coexisted. Injection into the superficial system was especially suited to the investigation of abnormalities in this area.

The venographic findings in patients with varicose veins due to incompetence of the superficial venous system varied with the level of injection and the degree of damage to the system. Percutaneous and cut-down polyethylene tube injections were carried out at all levels, including the proximal passage of a tube from a cut-down at the medial malleolus.

When percutaneous injection was made directly into a dilated and clinically incompetent varicose vein, total retrograde passage of the radiopaque medium was observed. The failure of proximal passage of the medium,

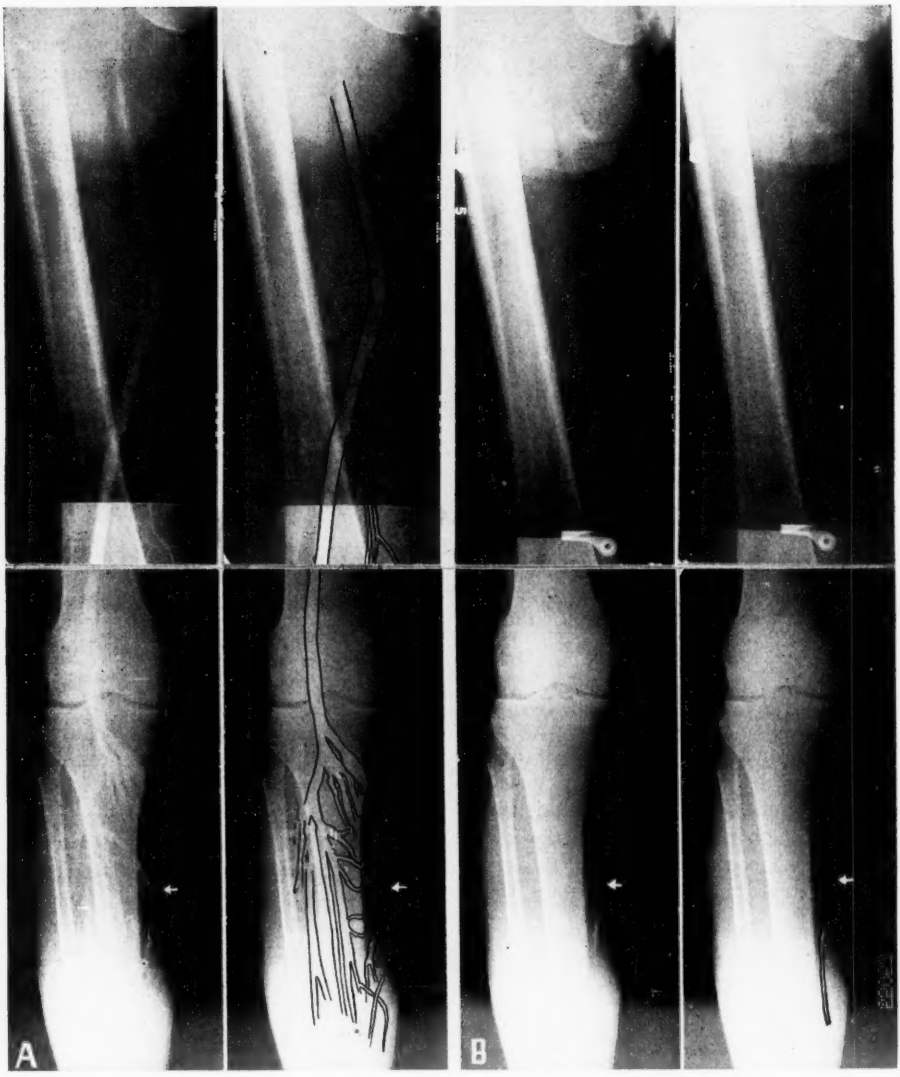


Fig. 1.—Functional venograms in a control subject with injection through a polyethylene tube which has been threaded up the greater saphenous vein from the ankle to the calf. The end of the tube is indicated by an arrow. Segmental passage of the medium from the superficial system into the deep is shown. As in previous studies, retouched roentgenograms are presented beside unretouched ones to delineate all veins opacified in the original films. The initial exposure is made in quiet dependency at the completion of injection. A second set of films under the leg and thigh are then exposed one minute later, after muscle exercise.

with total regurgitant flow, was regarded as true evidence of incompetency in contrast to the retrograde flow down normal-appearing veins, in which the major flow in quiet dependency was in a cephalad direction.

At times the retrograde flow of medium in quiet dependency was observed to be partially diverted into the deep system, and on other occasions it appeared to be unimpeded in its distal passage, with failure of the deep sys-

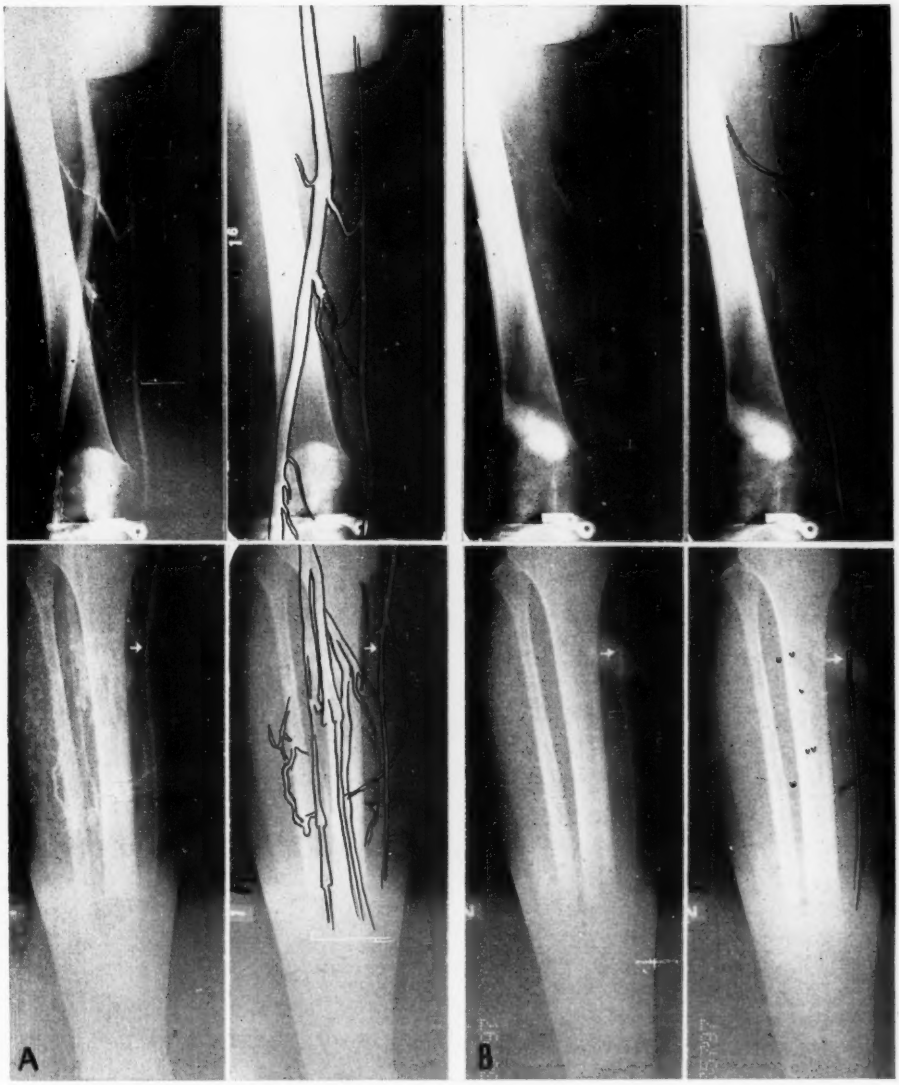


Fig. 2.—Functional venograms in a control subject with injection through a polyethylene tube. The tip of the tube is indicated by an arrow. Incomplete emptying of the superficial system with exercise is shown, in contrast to the clearing of the deep system.

tem to opacify. This observation is illustrated well by the divergent findings in the two extremities of a patient with bilateral varicose veins (Fig. 4).

Injection through a polyethylene tube inserted from the medial malleolus to the level of the lower calf often resulted in the accumulation of some medium in local varices at the level of the tip of the tube and in the retrograde flow back toward the ankle of the remaining medium. The force of injection was not sufficient to cause proximal flow of the material in the incompetent vein or to produce initial opacification of the deep sys-

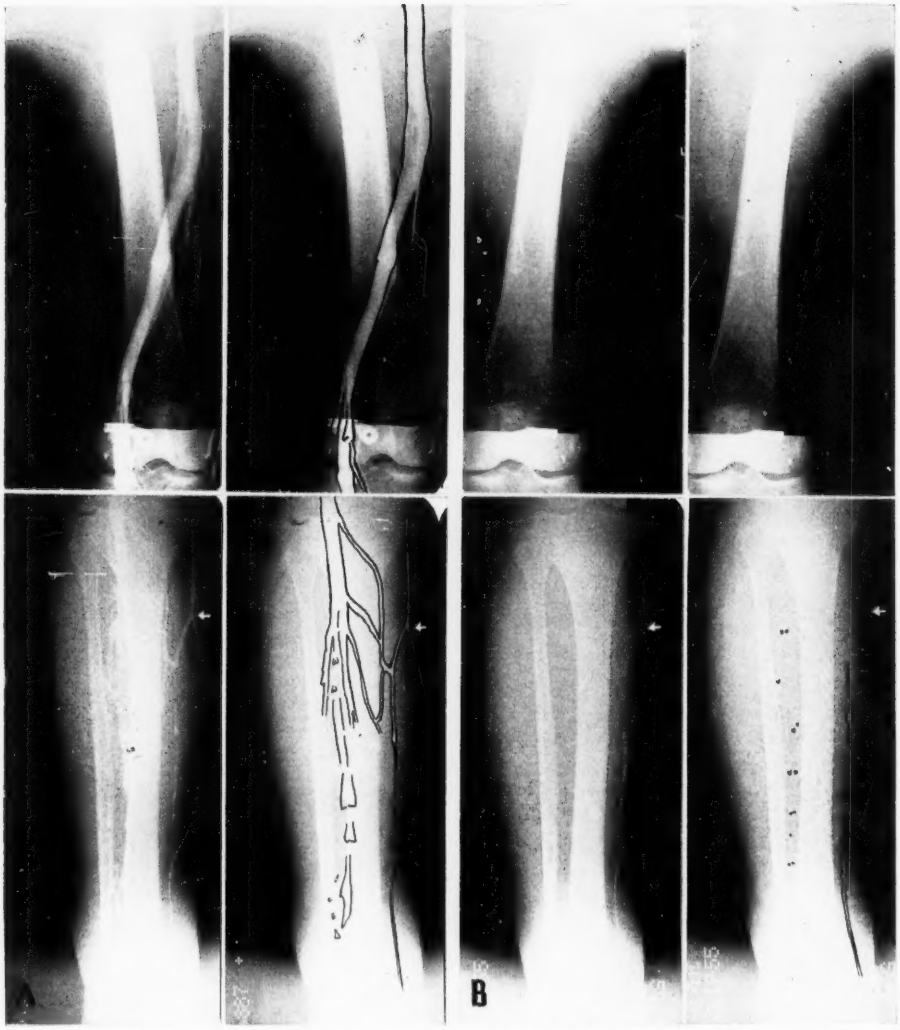


Fig. 3.—Normal superficial venograms in a patient with lymphedema. Injection is through a polyethylene tube threaded up to the calf (arrow) from the ankle.

tem in quiet dependency. The consistency of this observation depended, to be sure, on the level of the tip of the tube and on the degree of incompetency. By vigorous exercise, it was possible in some cases to produce opacification of the deep system, as is shown in Figure 5. In this case, massive regurgitation down a hugely dilated and tortuous greater saphenous vein is also demonstrated following popliteal-femoral trunk opacification.

In cases of superficial phlebitis or its sequelae, the capacity of the superficial system to carry venous blood and to clear with exercise appeared to be impaired. Although the superficial system normally clears less effectively with exercise than the deep, an even greater amount of radiopaque material tended to remain behind, seemingly immobile, in these cases. The proximal return

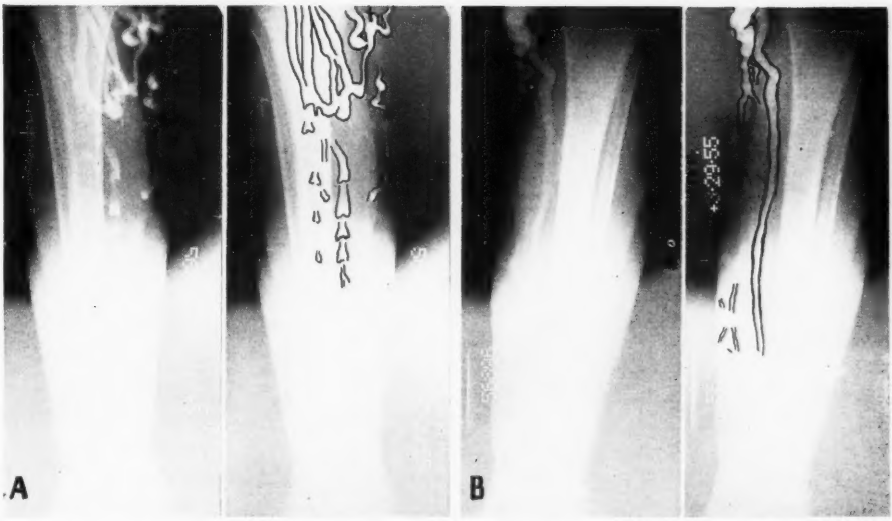


Fig. 4.—Roentgen findings in the leg on quiet dependency in a patient with bilateral varicose veins following percutaneous injection into enlarged and clinically incompetent superficial veins in the lower thigh bilaterally. The medium is largely diverted into the deep system on reaching the leg on the right side (*A*), whereas the distal flow on the left (*B*) is unimpeded, with failure of the deep system to opacify.

of venous blood was effected by passage into the deep system, which cleared with exercise.

The venographic findings in two cases have been selected to illustrate these observations. In one patient an acute episode of phlebitis and thrombosis involved some dilated and tortous veins on the lateral aspect of the lower thigh. One of the larger veins was divided under local anesthesia, and injection was carried out into the distal end by means of a polyethylene tube which had been secured within its lumen (Fig. 6). The dilated and tortuous nature of these veins is shown. The intraluminal clot gives the appearance of a double-contrast study. The bulk of the medium passed into the deep system and cleared with exercise. No change was produced by exercise in the roentgen appearance of the superficial veins which had been injected.

The second patient was studied by injection into a polyethylene tube which had been threaded up to the level of the upper calf from the middle malléolus. Approximately five months prior to injection the patient had had an attack of superficial phlebitis which began above the medial malleolus and extended proximally up the greater saphenous vein to the groin, with tenderness and evidence of inflammation along its route. Considerable branching of the greater saphenous system was shown (Fig. 7). The bulk of the medium was seen to pass segmentally through the communicating vessels into the deep system. There was some mild regurgitation in the deep system past several valve stations in decreasing concentration. This system cleared with exercise, with only tiny amounts of medium left behind in the valve cusps. Clearing of the radiopaque material with exercise from the network of superficial veins was poor.

DISORDERS OF THE DEEP SYSTEM

Radiopaque medium, when injected into the superficial system, will pass by communicating vessels in a segmental manner into the deep system in quiet weight-bearing dependency and up the popliteal-femoral trunk toward the heart. Once the medium has entered the deep system, a small amount of it often may pass downward past several

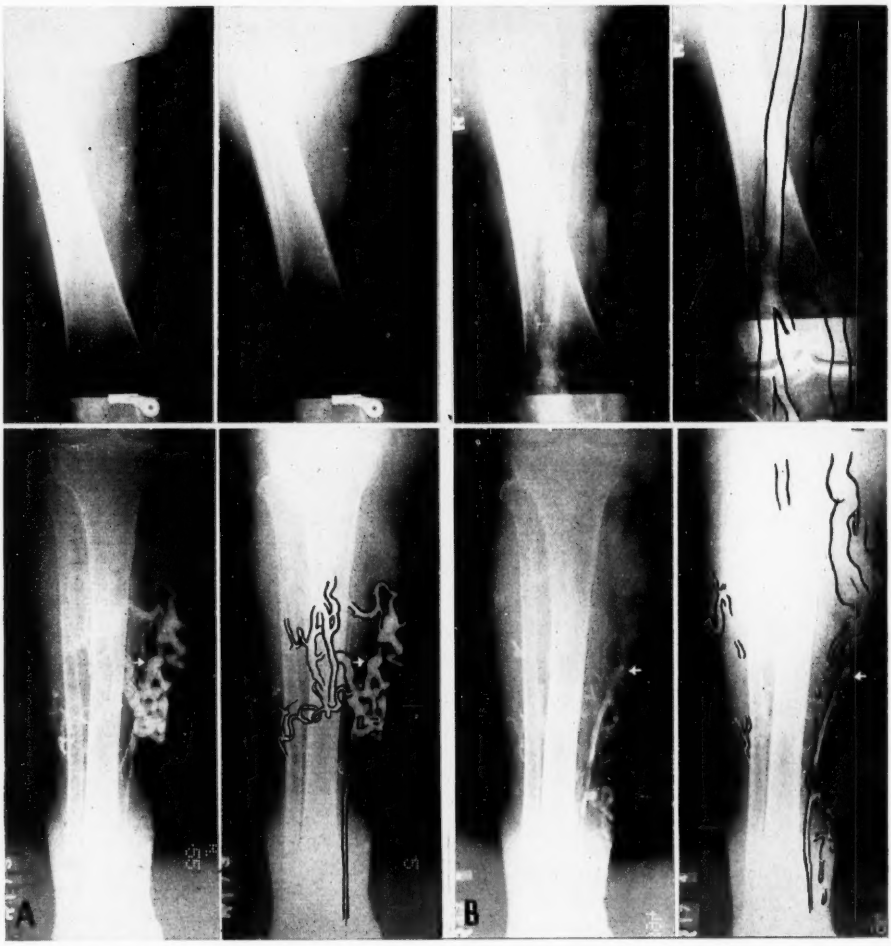


Fig. 5.—Venograms illustrating the findings on injection, through a polyethylene tube, into an incompetent greater saphenous system (arrow). There is no passage of medium into the deep system on quiet dependency. With vigorous exercise, the deep system is opacified and regurgitant spill of medium down a dilated and tortuous greater saphenous trunk is shown.

valve stations in decreasing concentration. With exercise, the medium will clear from the deep system. Occasionally, a tiny amount may remain behind in the cusps of some of the valves. This appears to be the normal mechanism for the return of venous blood from the superficial areas in the dependent limb. It has been observed repeatedly and consistently, and its validity provides us with a useful tool for the evaluation of the deep system as well as the superficial.

The deep system has failed to opacify with injection into the superficial system in the lower calf or higher only in those patients in whom the deep system was obstructed or when injection was made into a completely incompetent superficial vein with total, unimpeded retrograde flow. In the former instance, venous return is effected through the greater saphenous system, which opacifies in the thigh, as well as in the leg. Normal-appearing valves may be visualized, and the

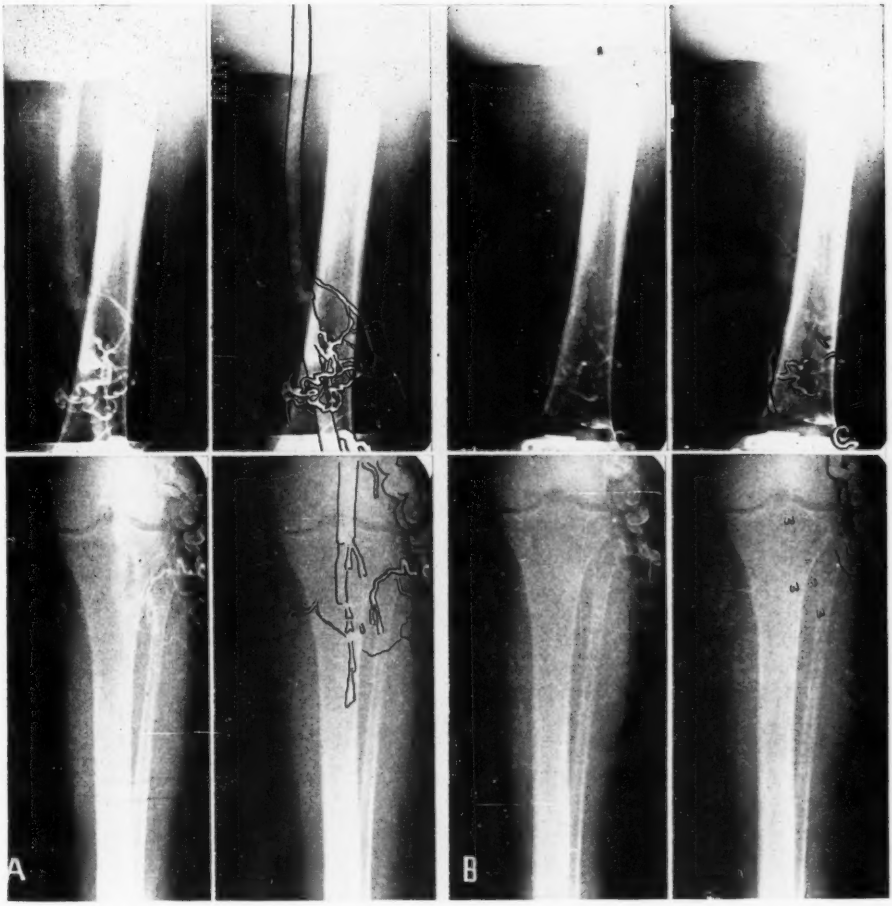


Fig. 6.—Venograms taken after injection above the knee through a polyethylene tube into a tortuous and dilated superficial vein with intraluminal thrombus formation.

veins tend to be straight rather than tortuous. These veins clear completely with exercise, even more effectively than do the superficial veins in control subjects without vascular disease. Although communicating vessels may be seen at various levels passing toward the anatomic location of the popliteal-femoral trunk, it is not opacified at any level before or after exercise. This finding is regarded as substantial evidence of deep venous obstruction. It has been shown elsewhere that this trunk, even when recanalized in the post-thrombotic state, will opacify in quiet dependency from superficial system injection, with proximal passage of the meduim and clearing with exercise.

Both acute thrombophlebitis and the post-phlebitic state were investigated. The majority of injections were made into the superficial system. Multiple injections at various levels into both superficial and deep systems were utilized in some patients on whom additional information was desired. One patient was seen because of vague complaints of discomfort and swelling in his leg. He was 38 years of age and otherwise in excellent health. Although there was no history of trauma or operation, thrombophlebitis of the

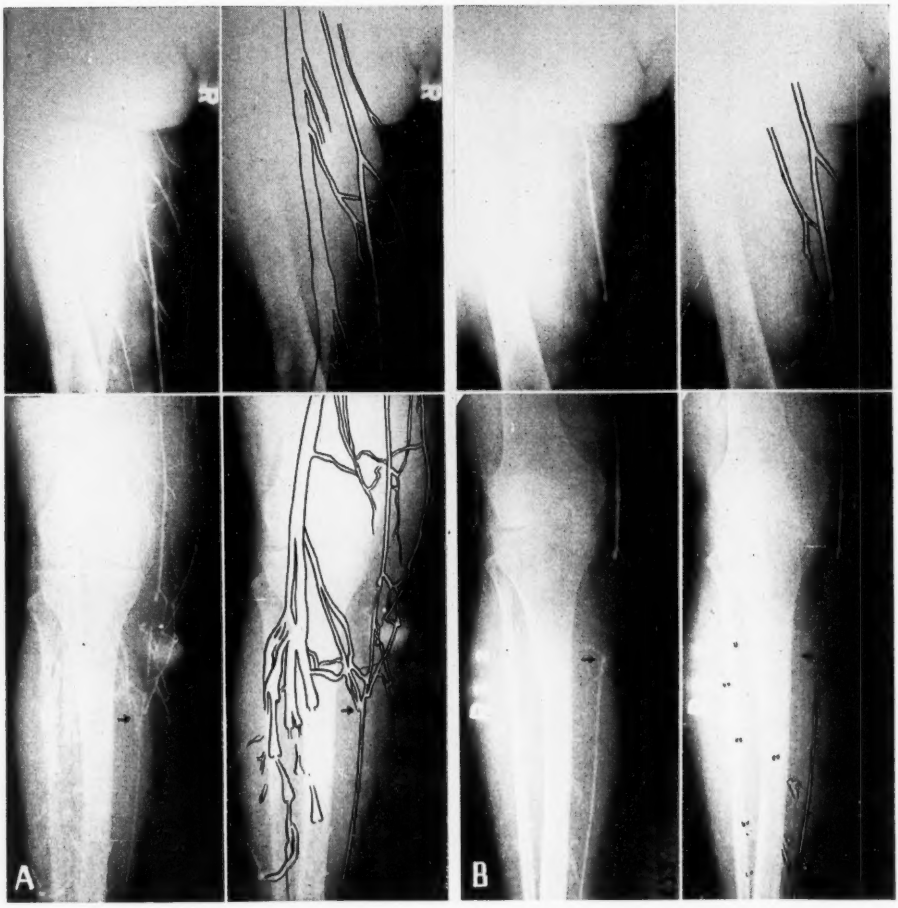


Fig. 7.—Roentgen findings on injection through a polyethylene tube (arrow) into a greater saphenous vein which had previously been involved in an episode of superficial phlebitis. The poor clearing of the branching greater saphenous system with exercise is demonstrated.

deep system was suspected. A polyethylene tube was inserted into a small superficial vein on the anterior aspect of the leg below the tibial tuberosity and was threaded medially. Injection was carried out through the tube in the routine manner (Fig. 8). It was found that the tip of the tube had just reached the lumen of the greater saphenous vein. There was some distal regurgitation past several valve stations, but the bulk of the medium had passed proximally against gravity. The medium cleared with exercise. At no time, before or after exercise, did the deep system opacify.

A localized area of obstruction in the femoral vein was demonstrated in another patient (Fig. 9). He was 36 years old and had had thrombophlebitis involving the right leg in 1941, after an appendectomy. Postphlebitic swelling persisted, and ulceration above the medial malleolus occurred with the passage of time. Approximately three years ago an operation, the exact nature of which is unknown, was carried out with an incision in the groin and several incisions below the knee. Following this procedure there was a marked increase in the swelling of the leg, with cyanosis. All of the incisions

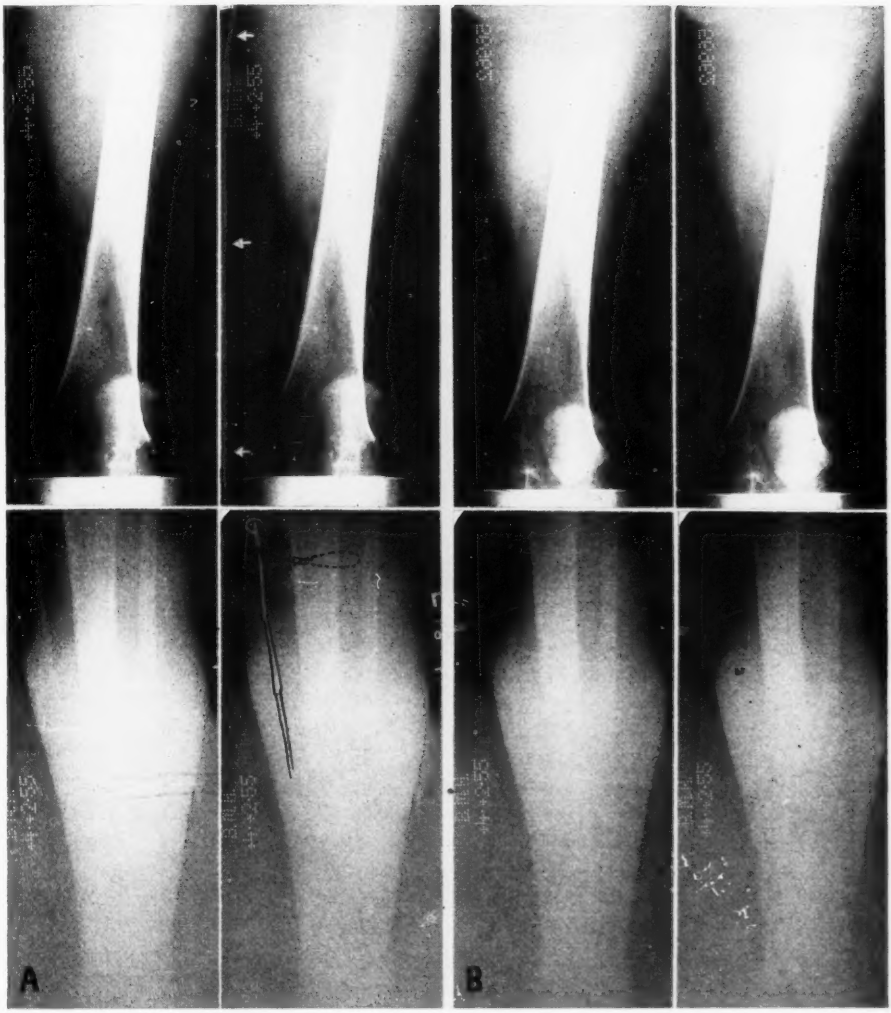


Fig. 8.—Functional venograms showing proximal passage of medium in the greater saphenous system, with failure of the deep system to opacify. Injection was made through a polyethylene tube (dotted line) which was inserted by cut-down into a dilated superficial vein on the anterior aspect of the leg and was threaded medially. The tip of the tube has just reached the lumen of the greater saphenous vein. The opacified greater saphenous vein in the thigh is indicated by arrows.

broke open, owing to the massive swelling. Although the leg survived, multiple ulcerations with excessive weeping and marked swelling persisted. Percutaneous injection into the popliteal vein revealed an obstruction at the lower portion of the femoral vein. The medium passed cephalad through collateral channels communicating with the profunda femoris and cleared with exercise. Identical findings were encountered on repeat popliteal injection three days later. Injection into the femoral vein at the inguinal ligament showed no retrograde flow.

In two patients attempts at percutaneous popliteal injection produced opacification in what appeared to be the profunda femoris

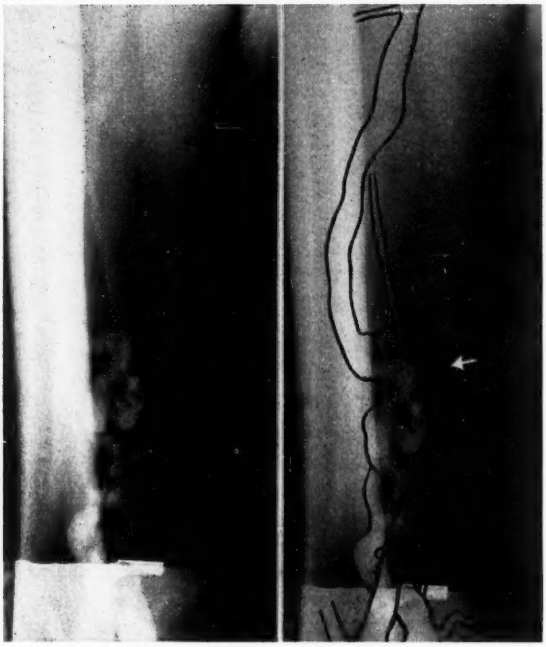
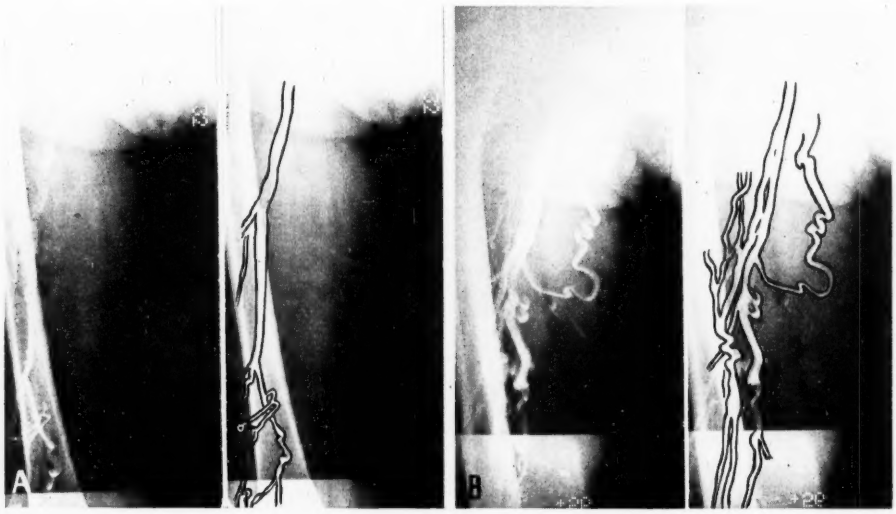


Fig. 9.—Roentgen demonstration of an obstruction in the popliteal-femoral venous trunk in quiet dependency. The radiopaque medium passed proximally through collaterals into the profunda femoris system. The medium was cleared with exercise.

Fig. 10.—Venograms of the thigh in two patients (*A* and *B*) taken in quiet dependency following percutaneous injection into the popliteal space. Both patients had had thrombophlebitis involving the deep system and had suggestive roentgen evidence of persisting deep trunk obstruction. The medium passed cephalad from the enlarged collaterals, into which the injection had been carried out, into the profunda femoris system and cleared with exercise.



system. One patient, studied one year after a postoperative episode of thrombophlebitis, was shown on superficial injection to have proximal passage of medium in that system with no opacification of the popliteal-femoral trunk. Careful probing of the popliteal space with a needle failed to puncture a venous space large enough to be the popliteal-femoral trunk. Injection was finally made into a smaller deep vein, which proved to be a collateral channel communicating with what appeared to be the profunda femoris system (Fig. 10*A*). The medium was cleared with exercise. The other patient was studied during an episode of phlebitis which involved the greater saphenous vein from the calf to the groin, with tenderness, induration, and pigmentation along its course. He had previously had thrombophlebitis of the deep system following an insect bite, with considerable firm swelling of the calf and pigmentation. An attempt was made to inject the medium into the popliteal vein percutaneously. It could not be located, and injection was carried out into a smaller deep vein, which, as in the previous case, proved to be a collateral vessel communicating with the profunda femoris system (Fig. 10*B*). The radiopaque material was cleared with exercise.

COMMENT

The problem of retrograde venous flow in quiet dependency is an important one, and its significance is in need of considerable clarification. Some authors, such as Bauer,[1] have regarded retrograde flow in quiet dependency as evidence of "idiopathic" incompetency and as an indication for deep venous interruption. My findings, on the other hand, in a large series of functional venographic studies carried out on both normal extremities and those with venous disorders, indicate that the absence of some retrograde flow in quiet dependency is more abnormal than its presence.

It has been shown that some retrograde flow in quiet dependency past one or more valve stations from the site of injection occurs in virtually all normal control subjects, whether the injection is into the femoral vein or the popliteal. Furthermore, when injection is made into the superficial system, retrograde flow often may be seen in the deep system several valve stations beyond the lowest visible communicating vessel. In patients in whom the deep trunk is obstructed and in whom the greater saphenous vein is serving as a major collateral for venous return from the dependent extremity, it is also found that some radiopaque material may drift downward from the site of injection in quiet dependency.

It appears that there are two important features which differentiate this normal type of regurgitant flow in quiet dependency from the total regurgitant flow seen in superficial venous incompetency with varicose veins. One is the observation that the bulk of the injected medium passes proximally against gravity even in quiet dependency. The medium which passes distally represents only a small portion of the total amount injected, and it passes distally in decreasing rather than increasing or uniform concentration. When medium is injected into a completely incompetent superficial vein in quiet dependency, there is total distal passage of the medium in uniform or increasing concentration and there is no proximal passage of the medium from the site of injection.

The second differential feature concerns the response to muscle activity. The normal vein clears practically completely with exercise, despite the occurrence of some retrograde flow in quiet dependency. Only tiny amounts of medium may be left behind in the valve cusps. In contrast, exercise does not produce proximal flow with clearing in the incompetent superficial vein. It is significant that a greater saphenous vein which is functioning as an important collateral because of obstruction in the deep system behaves in the same manner as a normally functioning deep vein. Despite the occurrence of some retrograde flow in quiet dependency, the major flow is cephalad and the vein clears with exercise.

When injection is made into a competent vein of the superficial system, the popliteal-femoral trunk has been observed consistently

to opacify if patent, even though recanalized. For this reason, the proximal passage of medium in the greater saphenous system in quiet dependency combined with failure of the deep system to opacify at any level is regarded as reliable evidence of deep venous obstruction. The potential value of this observation in evaluating the patency of the deep system in the postphlebitic state and in some of the more silent episodes of deep venous thrombosis is apparent. The only instances in which the deep system has failed to opacify when patent have involved injection into a totally incompetent superficial vein in which there was unimpeded regurgitant flow. Significantly, there was no proximal passage of medium in these cases from the site of injection in quiet dependency.

Radiopaque material which was injected into the deep system in cases of deep trunk obstruction appeared to pass cephalad in collateral channels communicating with the profunda femoris system. Indeed, the only instances of profunda femoris visualization with ascending rather than regurgitant flow of medium occurred with popliteal space injection in the presence of popliteal-femoral trunk obstruction. Presumably, the reason for this observation lies in the functional enlargement of the deep collaterals to a size sufficiently great to permit their puncture with relative ease by the needle used for percutaneous injection. Venous return through these collaterals was also demonstrated in one case in which injection was made into a popliteal-femoral trunk which was patent in the popliteal area but segmentally occluded from the lower thigh proximally. Although an insufficient number of studies of the deep system have been carried out after operative interruption of the femoral vein to justify any conclusion, it appears that segmental obstruction frequently follows ligation of the deep trunk, in contrast to the total obliteration of this trunk which occurs with acute thrombophlebitis. It would be of interest to learn of the status of the deep trunk and the nature of the deep venous collateral return in a significant number of patients from some of those institutions where there has been a large experience in the past with therapeutic and "prophylactic" femoral vein ligation.

From the studies reported here, it would appear that the superficial system in dependency serves principally as a collecting system for venous blood from the superficial area. The blood appears to pass segmentally into the deep system and to flow in it against gravity. Significant proximal return in the superficial system occurs only when there is obstruction of the deep trunk.

The degree of proximal flow into and up the deep trunk in quiet dependency emphasizes the importance of muscle tonus. It would be of interest, in this regard, to evaluate the role of muscle tonus in quiet weight-bearing dependency by the study of venous return from superficial injection in non-weight-bearing dependency and in limbs in which muscle tonus has been reduced by anesthesia or by paraplegia. It would also be of value to study the mechanisms of venous return in patients following bilateral thoracolumbar sympathectomy during the early stages of postural hypotension and later after compensatory adjustment.

More study is needed to clarify the mechanism of venous return when injection is carried out into the dorsum of the foot. There has been a tendency in a few cases for the medium to pool in concentration in the foot, with a collar-like area just above the malleoli. This is in contrast to prompt passage into the deep system when injection is made in the more muscular areas of the calf and thigh. Additional studies of this type on normal and diseased extremities may facilitate a better understanding of the frequent occurrence of stasis ulceration in the area above the medial malleolus. This is a dependent area where there is a concentration of superficial veins. It is, furthermore, a critical area of diminishing muscle support.

DISCUSSION

DR. ALTON OCHSNER JR., New Orleans: Did you use 70% Urokon, and do you think its use in the presence of an infected ulcer is likely to precipitate thrombophlebitis?

DR. THOMAS C. MOORE, Muncie, Ind.: I have used both 50% Urokon and 70% Urokon in a limited number of studies. It has been my experience that these more concentrated solutions have produced more patient discomfort, presumably from venospasm, than is desirable. I now use only the 30% Urokon and find it quite satisfactory. I am currently investigating the new Squibb product, Renografin, in both the 47.8% and the 59.7% concentrations. However, no comment can be made as yet on the suitability of this material. Phlebitis involving the superficial system has not been a problem in these venographic studies. There have been no deep venous or pulmonary complications.

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An Evaluation of Radical Surgery for the Post-Thrombophlebitic Syndrome

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and
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Scores of articles are published yearly relative to the post-thrombophlebitic syndrome. In these articles it is apparent that the therapy of the post-thrombophlebitic syndrome is still highly controversial. Many authors * advocate a conservative medical program. Others † claim that the surgical approach is the preferable one. The medical treatment usually includes long periods of bed rest or at least marked restriction of physical activity. As a result, many days of work and pay are lost. Conservative management at best is palliative only and certainly not curative. Nevertheless, the conservative medical program is all we have to offer and is adequate for the average post-thrombophlebitic case. We propose in this paper to advocate for the late and seriously crippling cases radical surgical treatment and are presenting an analysis of 60 patients so treated to substantiate our claims.

HISTORY

In 1941 Homans [4] brought out the idea of ligation or partial resection of the superficial femoral vein as the preferred surgical treatment for deep vein thrombophlebitis. Linton and Hardy,[5] in 1947, reported several cases in which a combined treatment of ligating the superficial femoral vein and ligation and stripping of the long and short saphenous vein were successfully undertaken for the treatment of the post-thrombophlebitic syndrome. Linton,‡ in a subsequent article, stated:

> In conclusion, it may be stated that although these results are not perfect, they demonstrate that in patients with the disease complex of the post-thrombophlebitic syndrome with ulceration, good to excellent results have been obtained in the majority of patients treated by: (1) Removal of the superficial system of veins of the affected lower extremity. (2) Interruption of the deep system of veins by ligation and division of the superficial femoral and its junction with the profunda femoris branch. (3) Interruption of the communicating veins on the inner and posterior aspect of the lower leg from below the knee. (4) Resection of the deep fascia on the posterior mesial aspect of the lower leg. (5) Wearing of an adequate elastic support as long as the edema of the extremity persists.

In 1948, Gunnar Bauer [6] advocated ligation of the popliteal vein instead of the superficial femoral vein in the treatment of post-thrombophlebitic sequelae. One of us,[7] in 1950, reported 12 cases in which a superficial femoral vein ligation and a high saphenous ligation and saphenous stripping were performed for the post-thrombophlebitic syndrome.

THE PATHOLOGIC PHYSIOLOGY OF THE POST-THROMBOPHLEBITIC STATE

An extremity that has been subject to deep vein thrombophlebitis is rarely ever normal again. Characteristic and often

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* References 1-3.

† References 4 and 5.

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grossly recognizable changes are usually present. The leg remains enlarged from ankle to groin. Lymphedematous swelling from ankle to knee occurs with standing. The thigh has a peculiar "thick" feeling. In late cases the skin of the lower leg is pigmented and atrophic. Leg ulceration is commonly present.

Venous hypertension present at the outset of the deep vein thrombosis persists in the post-thrombophlebitic state. As the vein recanalizes, the venous hypertension is transmitted via the communicating veins to the surface veins, and varicosities of the saphenous system develop. Venous stasis thus dominates the picture in the deep veins, communicating veins, and superficial veins. Furthermore, the venous hypertension is transmitted to the venous side of the capillary loop, and decreased arterial influx occurs. The resultant anoxia and the venous stasis lead to chronic malnutrition of the tissues and leg ulceration.

The lymphatic circulation becomes involved early in the post-thrombophlebitic state, the tubular lymphatics becoming obstructed by the inflammatory process in the femoral sheath. Confronted with excess edema formation as a result of the venous hypertension and tissue anoxia, the lymphatic system soon becomes decompensated. A protein-rich fluid accumulates in the soft tissues of the lower leg, frequently leading to subcutaneous fibrosis and episodes of cellulitis known as lymphangitis streptogenes. Extensive fibrosis and repeated episodes of cellulitis result in the classical end-stage of the postphlebitic state, the indurated leg.

COMPLICATIONS OF THE POST-THROMBOPHLEBITIC STATE

A. Stasis Dermatitis.—This condition results when resistance to infection is lowered by edema and impaired venous and lymphatic circulation.

B. Lymphangitis Streptogenes. — Fluid rich in protein collects in the lower extremities and is an excellent culture medium for bacteria. As a result, when there is a slight break in the skin of the foot, Streptococcus infection occurs, producing attacks of an acute erysipeloid nature. Sometimes the portal of entry is a fissure in the intertriginous skin between the toes occurring secondarily to epidermophytosis. Painful inguinal adenopathy accompanies the attacks because of ascending lymphangitis.

C. Stasis Ulceration.—There are ulcers in about 35% of patients with an indurated leg. This type of ulceration can be easily differentiated from the true varicose ulcer by the history of previous deep phlebitis and the appearance of the soft tissue changes. The ulcer is commonly seen in the lower part of the leg, mesial aspect, but may straddle the shin or even be present on the outer side of the leg. Postphlebitic ulcers are sometimes multiple, deep, and extremely painful. It is now believed that post-thrombophlebitic ulcers appear on the basis of two main causes: one, ischemia of the surrounding tissues because of a narrowing of the capillaries strangulated in the scar tissue and, two, a state of ambulatory venous hypertension due to the irreversible lesions involving the deep, superficial, and communicating veins (thickened, functionless, valveless veins).

D. Lymphedema of the Limb.—Lymphedema of the limb occurs in 100% of the cases of venous thrombosis. The lymphatic insufficiency results from local perivascular inflammation and the ensuing scar tissue and the lymphatic obstruction in the groin.

E. Varicose Veins.—When the deep venous system is incompetent, reflux is to the superficial venous system via the communicating veins. The superficial veins dilate, and their valves can no longer close. There is then a loss of the main feature of venous function—valvulation. The communicating veins around the ankle are particularly prone to dilate, because of great pressure at this area and minimal support to the vein wall. The superficial varicosities are often involved in episodes of chronic local phlebitis because of their close relationship to stasis dermatitis.

F. The Permanently Damaged Femoral Vein.—Irreversible and significant lesions occur in the femoral vein after deep vein thrombosis. The vein wall is thickened and intimately adherent to its vascular sheath and adjacent artery. The vein lumen is almost obliterated and practically always distorted (Fig. 1). The vein valves are nonexistent, owing to adhesions to the diseased vein intima. Clinically, the superficial femoral vein

Fig. 1.—Post-thrombophlebitic syndrome. Cross section of the superficial femoral vein. Recanalization has occurred, but the lumen remains distorted and partly obliterated. The vein valves are nonexistent.

looks like a solid white fibrotic cord. One readily recognizes that the patient has had a previous episode of deep phlebitis as soon as the vein is approached and its dissection begun.

H. The Pathologic Venous Circulation.—With the superficial femoral vein incompetent owing to valvular destruction and distorted vein lumen and the saphenous system incompetent owing to dilatation, blood flow

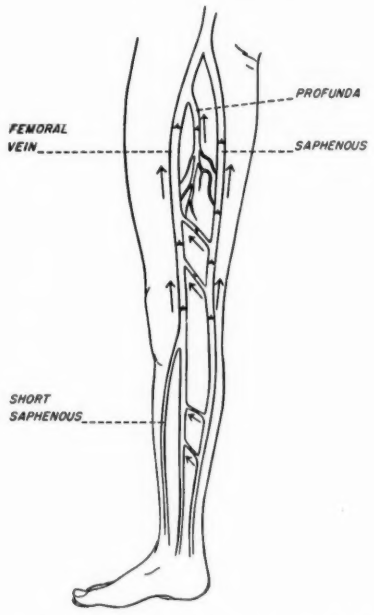

Fig. 2.—Normal venous flow via the saphenous, superficial femoral, and profunda femoris systems.

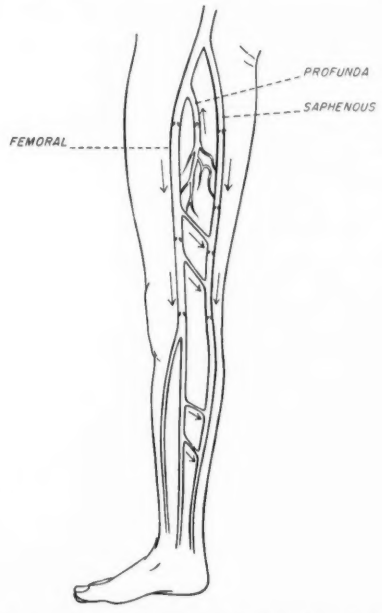

Fig. 3.—Venous flow in the post-thrombophlebitic syndrome. When the patient stands, coughs, or strains, venous flow is downward in the saphenous and superficial femoral systems.

is downward in the two great venous systems when the patient stands, strains, or coughs (Figs. 2 and 3).

SYMPTOMATOLOGY

The patient will present different symptoms according to the different stages of the disease. In the beginning, pain and swelling are the main symptoms. The pain is due to vasospasm. The pain often is of a causalgic nature and may be relieved by one or more lumbar sympathetic procaine (Novocain) blocks. The swelling is soft in the early stages but quickly becomes firm and hard. When an indurated leg develops, the patient complains of heaviness, fatigue in the leg, and cramping pains. Stasis dermatitis frequently develops. Episodes of sepsis, chills, and fever occur from minimum trauma or infection, owing to subdermal invasion of the lymphatics by streptococci. In addition, there are associated psychological factors. These patients are depressed and tend to reject medical aid when they are told of the chronicity of their condition and of the difficulty of obtaining good results even with the best treatments.

PRINCIPLES OF SURGICAL TREATMENT

The surgical treatment of the post-thrombophlebitic syndrome requires three stages of care: presurgical, the definitive surgical, and the postsurgical.

PRESURGICAL CARE

The presurgical care varies according to the associated complications. Marked edema calls for a period of bed rest with the foot of the bed elevated 12 in. Should cellulitis be present, voluminous wet dressings of saline solution or boric acid are applied to the affected part and antibiotics are given. Acute stasis dermatitis is similarly treated. Hydrocortisone is given when the dermatitis and cellulitis are aggravated by allergy.

The presurgical care of the post-thrombophlebitic ulcer includes the following steps: (*a*) complete bed rest with the foot of the bed elevated twelve inches; (*b*) culture of the ulcer and tests for sensitivity to antibiotics; (*c*) potassium permanganate 1:5000 for a half hour three times daily or continuous soaks of warm saline. This should be done until the acute infection clears. We do not wait for healing of the ulcer before undertaking surgery, feeling that this is needless loss of time.

DEFINITIVE SURGERY—RADICAL SURGERY FOR THE POST-THROMBOPHLEBITIC LEG

The surgery is composite in nature and may include one or all of the following procedures: long and short saphenous vein ligation and stripping, superficial femoral vein interruption, Homans' type of the Kondoleon procedure, excision of ulcer or devitalized skin and skin graft, lumbar sympathectomy.

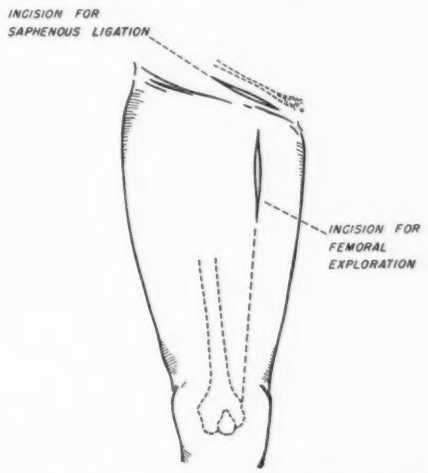

Fig. 4.—Surgery of the post-thrombophlebitic syndrome. The saphenous vein is exposed through a horizontal incision above the crease in the groin, and the superficial femoral, through a vertical incision in the upper third of the thigh.

The steps are described below:

A. Exposure of the Long Saphenous Vein.—A transverse incision is made in the inguinal region, usually just above the crease in the groin (Fig. 4). The long saphenous vein is exposed and lifted carefully from its bed. A chromic gut ligature is placed under the vein near the femoral junction, but it is not tied.

B. Exposure of the Superficial Femoral Vein.—This is done through a vertical incision over the upper anterior thigh region, deepening the incision through skin, subcutaneous tissue, and the anterior layer of Scarpa's fascia. The sartorius muscle is identified and retracted outwardly. The deep fascia is exposed and incised vertically over the pulsating femoral artery. With the index finger, the course of the pulsating femoral artery is constantly identified. The vascular sheath covering the artery is carefully split, and the superficial femoral artery and superficial femoral vein are dissected from one another. The dissection of the artery from the vein is usually a very difficult procedure, because the vein is attached to the artery by the chronic inflammatory process. Two steps may facilitate this procedure. With a 25-gauge needle, 1% procaine hydrochloride is injected into the sheath between the artery and vein. This decreases arterial spasm and facilitates the dissection of the femoral vein from the artery. Hyaluronidase (Wydase) solution on a cotton-tipped applicator has also been used with benefit. During this dissection, a tubular lymphatic vessel located on the anterior vein wall should be carefully avoided to prevent its injury. Any collateral veins adjacent to the femoral artery are spared to help carry on the circulation should the superficial femoral be tied. The dissection of the vein is directed upward until identification of the femoral profunda is established. The artery wall should never be clamped nor the artery retracted roughly. If the dissection proceeds along the mesial aspect of the vascular trunk, frequently the femoral vein can be freed from the artery without any handling or retraction of the artery. After dissection of the superficial femoral vein from the artery, the vessel is freed from the posterior bed by passing a smooth clamp under it. Two chromic 0 ligatures are drawn under the vessel, to be used during the venous pressure readings and to serve as future ligature of the vein.

C. Venous Pressure Readings (Fig. 5).—These are made to determine whether simultaneous ligation of the superficial femoral vein and the saphenous vein will cause postoperative venous hypertension. With use of a 20-gauge needle, the lumen of the femoral vein is penetrated distal to the femoral profunda. Venous pressure readings are taken according to the principles of Linton, with saline solution and an ordinary spinal manometer. First, a reading is taken of the uninterrupted superficial femoral vein; second, after temporary ligation or compression of the superficial femoral vein, and third, after temporary ligation of both the superficial femoral vein and the long saphenous vein. If the third venous pressure reading is twice as high as the first one (this event rarely occurs) or over 31 cm. of saline, both major venous systems should not be ligated. In this event, usually the superficial femoral vein is ligated and saphenous surgery is deferred to a later date. An adjuvant procedure to help interpret these venous pressure readings is to apply temporary pressure over the common femoral vein in the inguinal crease. The manometric pressure will usually rise quickly, indicating that the

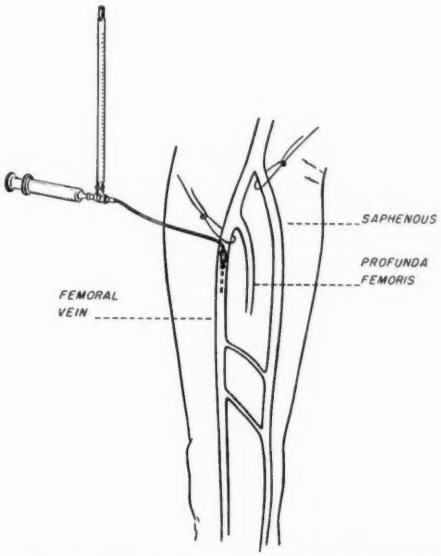

Fig. 5.—Surgery of the post-thrombophlebitic syndrome. Method of taking venous pressure readings with the saphenous and superficial veins temporarily occluded.

venous pressure apparatus is working properly and emphasizing the great venous hypertension that would be created if the common femoral vein were ligated. Rarely, the superficial femoral vein will be found occluded rather than recanalized and incompetent. In such instances, the venous pressure is taken in the saphenous vein only. Pressure of more than 31 cm. of saline with the saphenous vein temporarily ligated proximal to the needle indicates that the saphenous vein is needed for venous return and should not be sacrificed. A low reading indicates adequate collateral circulation via accessory veins along the femoral artery or via the femoral profunda. The saphenous vein can be ligated and stripped in such a case.

D. Ligation of the Superficial Femoral Vein and Long Saphenous Vein.—If venous pressure readings indicate that it is safe and practical, the superficial femoral vein should be ligated just distal to the entrance of the femoral profunda. A long stump should be avoided, because of the danger of clot formation. The long saphenous vein is then divided in the usual manner. The upper end is dissected to its junction with the common femoral vein and there ligated. All branches are ligated and divided with plain absorbable surgical (gut) sutures. The long saphenous vein is then removed from ankle to groin by use of internal or external vein strippers. Several incisions are made along the course of the vein to facilitate the stripping procedure. The short saphenous vein is similarly removed if varicosed.

E. Homans' Type of Kondoleon Procedure.—The purpose is to divide all incompetent perforator veins and to remove all pathologic skin, subcutaneous tissue, and contained varicosities and fascia in the lower leg. The extent of the induration is determined by palpation. A longitudinal incision is made extending from a few centimeters above the upper limits of the induration to a few centimeters below. The incision is deepened through the subcutaneous tissue and fascia onto the underlying muscle. Two fingers are inserted into the subfascial space. The fascia is split the entire length of the skin incision. The flaps are dissected back. The perforating veins, which are often very dilated in the post-thrombophlebitic syndrome, are clamped, divided, and ligated (Fig. 6). The fat, indurated tissue, and fascia are removed from each flap, leaving only a millimeter of subcutaneous tissue on the skin. This procedure is very difficult, the usually soft subcutaneous tissues being stony hard owing to calcific degeneration.

Fig. 6.—The incompetent perforator veins of the post-thrombophlebitic state as seen during the Kondoleon procedure.

The vitality of the skin is inspected, and all skin involved in chronic dermatitis or lacking vitality is resected. If the long saphenous vein has not been previously removed, it is now readily excised under direct vision. The wound is then irrigated with penicillin solution. Good hemostasis is obtained by clamping and ligating the smaller vessels. A Penrose tissue drain is applied through a stab wound through the lower flap. Interrupted fine gut sutures are used to approxi-

mate the thin rim of subdermal fat, and the skin edges are closed with 0000 black nonabsorbable surgical (silk) interrupted mattress sutures.

F. Excision of the Ulcer and All Bad Skin.—In most instances, the ulcer lies over the indurated area and is surrounded by damaged skin and fibrosed subcutaneous tissues. The surgery should be radical, excising the ulcer widely and also all indurated tissue under and around it and the underlying fascia. All pathologic skin is sacrificed, as diseased or devitalized skin invites recurrence. Good hemostasis is obtained by ligating bleeding vessels or applying pressure with hot sponges.

G. The Skin Graft.—With a Reese dermatome set for 0.010 to 0.012 in., a skin graft is removed from the thigh, and this is applied to the previously excised ulcer area. The graft is cut to pattern and fixed at four edges to the recipient area with fine silk stay sutures or towel clips. Interrupted 0000 silk sutures are used to affix the graft, the sutures passing through graft and skin so as to pile up the graft on the skin edge. The skin graft is further attached to the underlying bed with interrupted sutures of 0000 black silk. Several perforations are made to facilitate drainage. The dressing consists of one layer of thin scarlet red or petrolatum gauze, plain gauze cut to the pattern of the graft, mechanics' waste, and then a roll of ripple gauze. Finally a snug elastic (Ace) bandage is applied from toes to knee. A No. 16 F. rubber catheter is incorporated in the dressing, and the graft is moistened twice daily by the injection of 1 oz. (30 cc.) of glycerin (15%)-acetic acid (1%)-saline solution. A posterior plaster splint is applied if grafting has been about the ankle.

Several rules should be followed closely concerning skin grafts.

1. Do not expose tendons or remove the periosteum of bone when excising the ulcer. The skin will take best on the exposed muscle but will grow on tendon sheaths or periosteum.

2. Perfect hemostasis should be obtained in the bed of the graft before applying the graft.

3. The graft is sutured in place with the fewest possible stitches.

4. Thorough hemostasis of the donor site should be accomplished by compression by saline-soaked sponges before the permanent dressing is applied.

H. Lumbar Sympathectomy.—We perform a simultaneous lumbar sympathectomy should there be evidence of arterial insufficiency, excessive perspiration of the foot, or moist recurring dermatitis.

POSTSURGICAL CARE

The patient is returned from the operating room to a bed which has the foot elevated 12 in. Anticoagulant therapy is started immediately after the surgery, beginning with 200 mg. of bishydroxycoumarin (Dicumarol). Bishydroxycoumarin is given daily, according to the daily prothrombin time. It is continued for a few weeks after the patient leaves the hospital. Antibiotic therapy is instituted, usually with a penicillin-streptomycin preparation (Dicrysticin). Early ambulation is ordered unless skin grafting has been performed. Dressings over the skin graft are carefully changed on the eighth day, after the dressing is wetted with warm saline to prevent trauma. The graft is redressed with a single layer of petrolatum gauze and dry gauze, and the irrigations are discontinued. The stitches of the graft are removed on the 8th day; the stitches of the Kondoleon procedure are usually left in situ until the 12th day. The patient may begin ambulation on the 12th day with the use of elastic bandages.

If small areas of skin graft have failed to survive, these areas are resurfaced with Davis pinch grafts as soon as the condition is recognized. Before discharge from the hospital, the patient is given written instructions for the care of the extremity during the ambulatory period. Emphasis is placed on the avoidance of leg swelling. Excessive drying of the graft is prevented by the occa-

sional application of cold cream with wool fat (lanolin) or boric acid ointment. Approximately three or four months of meticulous postoperative care are required to protect the graft until it has become of normal color and texture and able to withstand the stress and trauma incident to normal living.

REVIEW OF SIXTY POST-THROMBOPHLEBITIC CASES TREATED SURGICALLY

During the past five years we have had 60 cases of advanced post-thrombophlebitic syndrome in which radical surgery was employed. The extent and type of surgery has varied according to the existing pathology, but a superficial femoral vein ligation has been common to all. The composite procedure has often included a ligation of the superficial femoral vein, a ligation of the long saphenous vein with resection of this venous system by stripping technique, Homans' type of the Kondoleon procedure, an excision of the ulcer or devitalized skin, a skin graft, and a lumbar sympathectomy. Tabulation of the surgical procedures performed follows:

	Cases, No.
A. Ligation of the superficial femoral vein; ligation and stripping of the long saphenous vein	25
B. Ligation of the superficial femoral vein; ligation and stripping of the long saphenous vein and an associated Homans' type of Kondoleon procedure	13
C. Ligation of the superficial femoral vein; ligation and stripping of the long saphenous vein; excision of ulcer and skin graft.	8
D. Ligation of the superficial femoral vein; ligation and stripping of the long saphenous vein; Homans' type of Kondoleon procedure, excision of ulcer and skin graft	14
TOTAL	60
E. Lumbar sypathectomy for concomitant arterial insufficiency or to facilitate skin grafting	10

Simultaneous lumbar sympathectomy or subsequent sympathectomy and regrafting were performed in 10 cases. The indications for sympathectomy were concomitant arterial insufficiency and sloughing of the graft. The short saphenous vein was also ligated below the popliteal space and resected from this area to the external malleolus when varicosed. During the past two years, our tendency has been to do more skin grafts, removing widely skin involved in chronic dermatitis or recurring episodes of local phlebitis or small ulcerations.

RATIONALE OF SUPERFICIAL FEMORAL VEIN LIGATION FOR THE POST-THROMBOPHLEBITIC SYNDROME

Vein function, when the extremity is in the dependent position, depends on active motion and valvulation. Valve function is negligible in the superficial femoral vein, once it has been involved in thrombophlebitis. One has only to dissect the vein out a few times to become convinced that it is invariably a thick white cord, almost resembling a large nerve, that it has an irregular and distorted lumen, and that its valves are absent or deformed (Fig. 1). Blood, at best, can only flow slowly up such a vein in the resting position, or even with walking. When the patient coughs, strains, or stands there is unquestionably a reflux down the superficial femoral vein, overloading the veins of the lower extremity with blood. Venous hypertension in the lower leg is thus produced. We feel that this is the explanation of the large incompetent perforator veins and the extensive varicosities of the saphenous system that develop in the post-thrombophlebitic state (Figs. 2 and 3). If one accepts this explanation of the cause of the enormous varicosity of the late post-thrombophlebitic state, one must accept the rationale of superficial femoral vein ligation in the therapy of these advanced cases.

It should be said here that many authors have recently indicated that they consider superficial femoral vein ligation for the cases under discussion irrational, and some authors who formerly advocated the procedure are now opposed to it. The trend away from superficial femoral vein ligation is the result of walking venous pressure studies as reported by DeCamp and his associates and

descending venography studies as reported by Shumacker. Pertinent excerpts from the literature are given below:

A. DeCamp, Schramel, Ray, Feibelman, Ward, and Ochsner,[8] in two patients with the post-thrombophlebitic syndrome, made studies before and after ligation of the superficial femoral or popliteal vein and demonstrated a sharp increase in ambulatory venous pressure.

> Ligation of deep veins of the leg for chronic lower leg conditions must be considered an experimental procedure. All reported evidence to date indicates that it has an adverse effect on the venous hypertension in the leg. We are forced to reverse our previous opinion and conclude that deep vein ligation for chronic conditions of the lower leg is, on the basis of present evidence, not indicated except to prevent recurrence of embolic phenomena.

B. Shumacker[9]:

> They [venographic studies] have helped to clarify certain problems of therapy in the postthrombotic state by demonstrating that the recanalized vein, contrary to generally held opinion, does not contribute to venous stasis by permitting regurgitant flow of blood. On the other hand, in spite of its distorted and valveless lumen, it contributes to the proximal propulsion of blood.

C. De Takats[10]:

> A deep vein is an important afferent channel, and even if it does frequently recanalize after an old thrombosis leading to incompetent valves, regurgitation of blood on standing is still preferable to obstruction of a main draining channel on exercise.

D. Martorell[3]:

> However, it is generally accepted that ligation of the venous system, particularly the deep vein can not only be useless but harmful. It is evident that a venous ligation cannot act as a venous valve. Insufficiency of the valve is the cause of venous stasis only while in the vertical position. Venous ligation disturbs circulation at all times and in any position. To cure the disease, the deep valvular insufficiency, with another disease, venous obliteration would not give satisfactory results. On the contrary, extirpation of the voluminous and insufficient internal saphenous, which occurs as the result of phlebitis has always given me good results in the treatment of the postphlebitic ulcer.

E. Mahorner[11]:

> My own personal experience and viewpoint is that never is a deep vein ligated with impunity.

We certainly agree that surgery has no place in the therapy of the average post-thrombophlebitic case. When edema is reversible and disappears overnight, when large varicose veins are absent, when skin changes are not advanced, when excessive subcutaneous fibrosis is absent, and when there is no indolent ulceration, a conservative program is the best form of treatment. In this paper, however, we are concerned with late and advanced cases, disabled for years by their post-thromophlebitic complications. They are the cases in which the "venous reflux" element of the post-thrombophlebitic state is prominent rather than the "lymphatic obstruction component." The venous reflux component is evaluated and the cases are selected on the basis of the clinical appearance and on the venous tourniquet test applied below the knee, as described by Linton. In most instances intensive medical management had repeatedly failed. These are the cases we had undertaken to rehabilitate by radical surgery. The superficial femoral ligation is only one phase of the composite surgery we have performed, but we continue to include it when (1) there is evidence of marked incompetence of the communicating veins and the secondary varicosities are enormous and (2) when there is large indolent ulceration.

Our reasons for continuing to include superficial femoral vein ligation in our multipronged attacks on advanced post-thrombophlebitic disease are the following:

1. At surgery, the gross appearance of the superficial femoral vein is such as to give the impression that it is valueless for vein function.

2. Our cases have failed to show evidence of venous hypertension or venous stasis over a long follow-up period. One would expect some violaceous discoloration of the skin, the late development of varicose veins or phlebectasias, the persistence or increase of edema if this were the case. When true venous hypertension develops in the lower extremities, the tendency to form varicose veins is enormous. Witness the large vari-

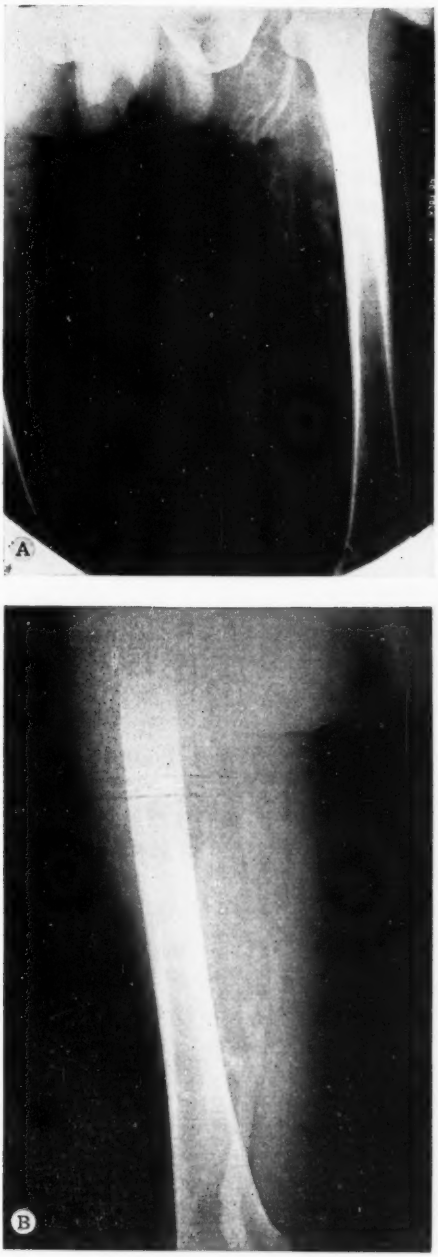

Fig. 7.—Postsurgical venograms. The superficial femoral vein has been ligated, and the saphenous vein has been ligated and stripped. Adequate venous return is visualized via the smaller veins in the thigh and the profunda femoris vein.

cosities that develop during pregnancy in spite of a previous well-performed saphenous ligation and stripping.

3. Where there is a high-grade venous obstruction, active ambulation increases the edema. This is because the venous outflow track competent to handle the volume of blood flow at rest is unable to handle the greater volume of flow incident to exercise. In our cases, exercise has helped the circulation, reduced the tendency to edema, and increased the comfort of the patient.

4. In a few postoperative venograms (Fig. 7) we have been able to demonstrate that the venous blood ascends the leg through the popliteal vein and the superficial femoral to the lower third of midthigh. It then passes through small muscular branches to enter the femoral profunda and then on to the common femoral and the pelvis. We have not encountered marked dilatation of this collateral venous circulation after surgery. This return flow through the smaller collateral veins is as desired and seems entirely adequate.

5. In several of our early cases a composite operation was performed but the superficial femoral vein procedure was omitted. Recurrence of disability (post-thrombophlebitic induration or small ulcerations) led to a second procedure including a superficial femoral vein ligation, with definite benefit.

6. The varicosities of the post-thrombophlebitic state are a late development—often occurring many years after an initial episode. This fits in with the hypothesis that they are the result of venous hypertension, created by downward flow in the superficial femoral vein, and reflux through the communicator veins. This would suggest that a superficial femoral vein ligation is as important in preventing reoccurrence of the varicosities as is the ancillary ligation and stripping of the saphenous system.

7. The superficial femoral vein ligation has given added protection against pulmonary embolism following such extensive surgery. This has often been a source of comfort to us.

The crux of the question of superficial femoral vein ligation rests in the status of the common femoral vein and the smaller collaterals in the thigh. In those rare instances in which the common femoral vein fails to recanalize, even the saphenous system cannot furnish an adequate venous outflow, the blood returning to the superior vena cava via the superficial collateral veins of the abdominal wall. In such a situation even eradication of the varicosed system would seem to be contraindicated. But frequently in cases of persistent occlusion of the common femoral vein we have observed a substantial collateral vein running along the anterior wall of the femoral vein. In such cases, venous pressure readings—now taken in the temporarily occluded varicosed saphenous vein—have indicated that the saphenous can be eradicated, and we have done this, with marked improvement of the patient.

If the common femoral vein has recanalized and is patent, it will furnish an adequate conduit for venous return via the femoral profunda vein and the superficial femoral vein can be sacrificed with impunity (Fig. 8). The occasional patient who has developed increased edema immediately after combined superficial femoral ligation and ligation and stripping of the saphenous vein probably does so because of (1) poor selection of case; (2) congenital inadequacy of collateral venous channels, or (3) postoperative thrombosis of some of the collaterals.

All of our cases are maintained on anticoagulant therapy postoperatively.

It has been hard to evaluate the actual benefit that can be ascribed to superficial femoral vein ligation in our series, for our surgery has usually included a composite procedure, aiming at eradicating all of the abnormal physiology and pathological tissue. We certainly do not feel that venous ligation of any form benefits lymphedema, but it has not, in our experience, increased lymphedema when performed for the indications listed. And it seems to have contributed definitely to the composite surgery for the disease. The 60 cases we have carefully followed up and herein report would indicate that superficial femoral vein ligation in the post-thrombophlebitic state has produced no untoward sequelae and has done considerable good. Lest we be misunderstood, we do not advocate superficial femoral ligation for the early uncomplicated post-thrombophlebitic cases or for post-thrombophlebitic lymphedema. Its use should be restricted to later cases presenting extensive secondary varicosities, incompetent perforator veins, and post-thrombophlebitic leg ulceration.

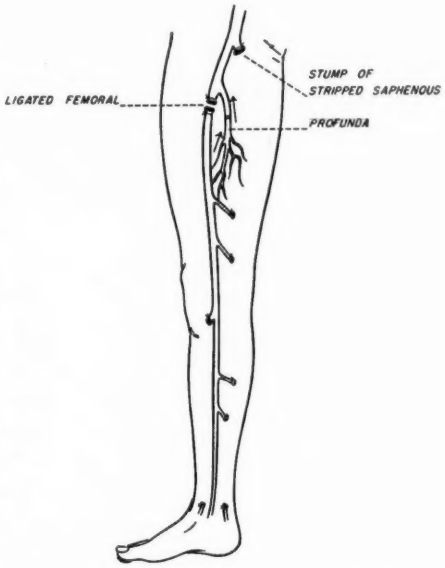

Fig. 8.—Diagram of the venous circulation in the post-thrombophlebitic state, after superficial femoral vein ligation and stripping. Venous return is by means of the small branches in the thigh and in the profunda femoris.

These are probably the only cases that have developed enough collateral venous circulation to permit the procedure without untoward results.

COMPOSITE PROCEDURES AND THOROUGH SURGERY—THE KEY TO SUCCESS

We have indicated above that we have felt that superficial femoral vein ligation has contributed much to the management of the post-thrombophlebitic state. On the other

hand, we feel that most important are the several procedures used to eradicate completely the existing pathological tissue, the removal of the varicosed saphenous system, and the interruption of the incompetent perforator veins. Our percentage of success increased as our surgery became more radical. Recurrence of disability often resulted from overlooking a few varicosities, from not making the Kondoleon procedure extensive enough, from failure to excise widely and completely all of the chronically diseased or devitalized skin, from too small a skin graft, or from failure to interrupt all communicator veins. A Kondoleon procedure from knee to ankle will heal just as readily as a short one in the lower third of the leg and will give far better results. A skin graft over a large area of the leg will take even more quickly than a small graft placed in a bed surrounded by scar tissue or chronic dermatitis. Should the pathology be so extensive as to require a staged procedure, this should be included in the planning, and the case should not be dismissed until all phases of the procedure have been performed. Should extensive failure of the skin graft occur, often a regrafting with simultaneous sympathectomy will bring about success. Large fatty pads above and below the malleoli are advisedly removed. Often the only area that will swell after surgery will be here.

EVALUATION OF RADICAL SURGERY FOR THE POST-THROMBOPHLEBITIC STATE

In order to evaluate the long-term results of radical surgery as outlined above for the post-thrombophlebitic state, we have followed up an unselected series of 60 cases. A minimum of two years and a maximum of five years have elapsed since the surgery. The questionnaire was filled in either by the patient or by ourselves. Over 50% were personally interviewed.

Generally speaking, the results we have obtained can be considered good. The great majority of the patients were more comfortable and were very pleased with their limbs. Many patients, previously invalided by their extremities, have been restored to an active life.

Swelling.—Forty-five of the patients stated that after operation the swelling had been much less than before. Nine patients felt that their swelling was worse. Four of these represent an error in selection of patients, for the preoperative lymphedematous component was pronounced rather than the venous reflux component. As stated above, a superficial femoral vein ligation is contraindicated for this group. The other five carried out the postoperative instructions poorly. They were unwilling to accept the need of wearing a strong elastic support at all times. In three cases the swelling was approximately the same as before surgery. Forty-three of the patients followed closely the instructions to wear either a strong elastic bandage or a similar stocking. These patients have reported that their swelling is much more readily controlled than prior to surgery. This we consider important, for once normal skin has been placed on normal muscle, by the procedures outlined in this report, the patients can wear their supports with relative comfort and the edema can be actually contained without great difficulty.

Recurrence of Ulceration or Breakdown of the Skin Graft.—Of the 22 ulcer cases, there has been a breakdown of the skin graft or recurrence of ulceration in 5. The areas involved were usually small and were readily managed by compression bandages or regrafting.

Recurrence of Varicose Veins.—The secondary appearance of superficial varicosities has been notable by its absence. Over years of follow-up in cases in which the surgery was adequately performed in the initial procedure, it has not been necessary to perform again a saphenous ligation or stripping. Only rarely have a few injections been necessary for localized varicosities. As mentioned above, we have seen no evidences of venous hypertension as a late sequela of this series.

Leg Ache.—The great majority of the patients were emphatic in their statements that

their extremities were much more comfortable.

SUMMARY

A review of the history, pathological physiology, and complications of the post-thrombophlebitic state is presented. Conservative management is recognized as the best treatment for the average post-thrombophlebitic leg. Contrary to the opinion of some extremely active surgeons in this field, we advocate radical surgical treatment for most of the cases presenting the more serious complications of the post-thrombophlebitic syndrome. Our surgical procedures are described. These include saphenous vein ligation and stripping, Homans' type of the Kondoleon procedure, interruption of the incompetent perforator veins after the method of Linton, wide excision of the ulcer and devitalized skin, and extensive skin grafting. It is our belief that simultaneous performance of all of the surgical procedures indicated is more important than any one procedure.

We continue to perform superficial femoral vein ligation in conjunction with the other surgical measures when the venous reflux component is great. If one is to accept, as the cause of the large secondary varicosities of the post-thrombophlebitic state, venous reflux via the superficial femoral vein and communicators, one must accept superficial femoral vein ligation as logical in the treatment of these cases. Superficial femoral vein ligation is contraindicated when the chief sequela of the post-thrombophlebitic syndrome is lymphedema.

Sixty cases having had radical surgical treatment for the post-thrombophlebitic syndrome have been followed up, and the clinical results are presented. Radical surgery results in eradication of the diseased skin, of the fibrosed and indurated subcutaneous tissues, and of the contained varicosities. The incompetent communicator veins are effectively interrupted, and the reflux down the diseased femoral vein and down the varicosed saphenous vein is prevented. Leg ulceration is effectively cured. After radical surgery the patient has a limb with normal skin resting on well-vascularized normal muscle. Recurrence of leg ulceration is minimal and rare, and the slight lymphedema that persists is now readily controlled and comfortable. Again, it is well to remember that no matter how bad a post-thrombophlebitic or venous stasis leg appears, there is a normal leg underneath at the muscle level. Our conclusion is that radical surgery is far superior to medical management for the seriously disabled post-thrombophlebitic leg.

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Obliteration of Varicose Veins by the Intraluminal Suture Technic

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An incompetent saphenous vein may be obliterated by various means. Retrograde injection with sclerosing solutions was originally believed to be a simple and hazardless procedure.[1] Boyd [3] has shown that radiopaque contrast medium with the sclerosing agent, injected into superficial varices, enters rapidly into the deep venous system, where it probably has a deleterious effect. For this reason we have believed the injection of massive amounts, 5 cc. or more, of sclerosing agents should be abandoned.

Abraham [4] reported upon the use of a silk thread introduced into the lumen of the saphenous vein to cause thrombosis and ultimate obliteration of the vein. This is a report of further experience with similar techniques.

METHOD

The entire limb is cleansed and prepared for surgery with a hexachlorophene (*p*Hiso-Hex) scrub the evening before and just prior to surgery. The skin incision and high saphenous ligation are done after the method of McPheeters.[2] A vein stripper with a small olive tip is threaded down the lumen of the greater saphenous vein. An incision is made over the tip of the stripper exposing it. The distal segment of saphenous vein is then ligated. The suture to be placed into the lumen of the vessel is tied to the tip of the stripper and the stripper removed in a retrograde fashion without stripping the vein. The stripper is cut free of the suture, transfixed, and tied through the ends of the vein. A second ligation of the saphenous is done farther in on the vein segment from each end (Fig. 1). This step is important to prevent bleeding from the cut ends of the saphenous vein. One must also be careful not to pull the intraluminal suture too tightly, thus reefing the vein on the suture. This may cause a pulling sensation of which the patient

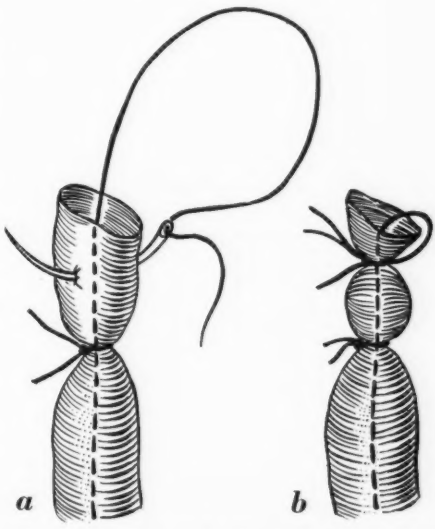

Fig. 1.—Method of fixation of the intraluminal suture and terminal ligation.

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National Heart Trainee, U. S. P. H. S. (Dr. Murphy).

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may complain in the postoperative course. We have interrupted the intraluminal suture at the knee in some instances, to assure that the vein is not reefed on the suture and in order to use this technique in more than one venous channel in the medial aspect of the leg.

The incisions are closed in a routine manner without special consideration. A snug elastic bandage is applied from the toes to the groin and left in place for 10 days. We have found an Elastoplast dressing to be advantageous as a substitute for the cloth bandages. Penicillin is given the day of surgery as a prophylactic measure.

Local, spinal, or general anesthesia was used. A 1% procaine hydrochloride solution was used for local anesthesia, supplemented by 50 mg. of meperidine (Demerol) hydrochloride, given intravenously just prior to the passage of the vein stripper.

In the postoperative period the patient is encouraged to be as active as possible. Sitting is discouraged. Good elastic support is applied to the legs from the toes to the knee after the initial dressing is removed. We have found the rubber reinforced elastic bandage to be satisfactory until all edema and pain are gone.

RESULTS

Thirty-one procedures are included in this report. There were seven males and 24 female patients. The ages ranged from 21 years to 76 years, the mean being 68 years. All patients had incompetency of their greater saphenous system, five had lesser saphenous incompetency, eight had incompetency of their communicating veins, and five had a history of large stasis ulcers. All patients with open ulcers were treated by conservative therapy until the ulcers were healed.

Two types of intraluminal suture were used, 00 absorbable surgical chromic (gut) suture and black 000 nonabsorbable surgical (silk) suture. The average hospital stay with the silk suture was six days and three and three-fourth days with the chromic suture. This average hospital stay is misleading, however, as patients were often held in the hospital for study reasons. The last four patients in this series were not hospitalized but had the procedure as outpatients. Eleven patients were discharged either on the day of surgery or on the morning after surgery.

After this procedure, 17 of the 31 patients experienced a moderate amount of pain along the course of the saphenous vein, especially at the knee. This occasionally caused transitory contractures at the knee. The pain and contracture were usually gone by the 10th postoperative day and at no time limited activity severely. All of these contractures were found in patients in whom a chromic suture was used as the intraluminal agent. None of the patients in whom silk suture was used experienced pain or contractures. There were no instances of long-term contracture or of persistence of pain. As a control, two patients had the passage of the stripper without insertion of a suture in the vein. In one of these patients the vein thrombosed only at the knee, and she developed a contracture for about 10 days. In the other patient, no change was noted postoperatively.

Sixteen of the thirty-one patients showed a mild elevation of temperature from one to four days postoperatively. It ranged from 99 to 101 F, returning to normal by the fourth postoperative day. Two patients experienced severe fever and chills. One patient had a daily temperature elevation to 104 F for 10 days. At that time a superficial femoral-vein ligation was done. The course after this was uneventful. A second patient had temperatures to 102 F for seven days after surgery, which returned to normal on antibiotic therapy. The etiology of the fever in these cases is obscure. Bacteremia or sensitivity to the long intravascular suture must be considered. Repeated blood cultures in these cases were all sterile.

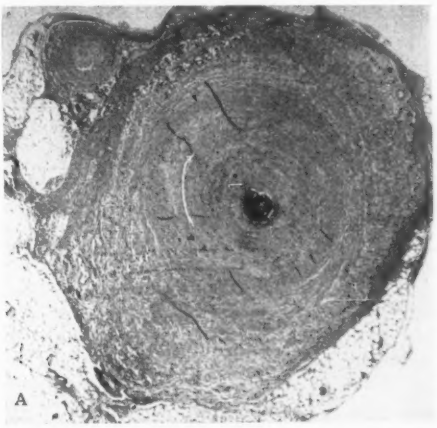
The average time of return to normal activity was three and one-half weeks. After this time, the patients had neither signs nor symptoms referable to this surgery. The range was from two to six weeks.

Late Follow-Up.—These patients have been followed from 10 to 28 months. There has been no evidence of recanalization of the thrombosed veins. The evaluation for oblit-

eration of the vein by this technique is demonstrated by Figures 2 and 3.

Complications.—Three patients had complications. The two patients with hyperpyrexia are discussed above. One patient in whom a 00 nonabsorbable surgical (silk) suture was placed from the groin to ankle developed a large chronically infected sinus at the knee. This was explored without anesthesia and the suture removed. This latter patient had a low-grade mycotic infection in the skin of the foot and ankle when operated originally and may have been infected from that source at surgery.

Fig. 3.—Photomicroscopic cross-section of a saphenous vein obliterated by an intraluminal chromic suture. There has been hyaline replacement of the suture material.



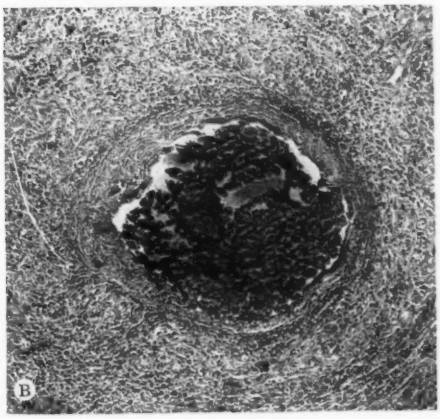


Fig. 2.—*A*, photomicroscopic cross-section of the saphenous vein obliterated by a silk intraluminal suture. *B*, high power of the intraluminal silk suture showing organization about the suture.

COMMENT

This study shows that an intraluminal absorbable surgical (gut) suture is a satisfactory means of causing a local thrombosis and obliteration of a venous lumen. The induced saphenous thrombophlebitis runs the typical course of that disease, with mild fever, pain, and occasionally a mild temporary contracture at the knee. These symptoms usually disappear by the 10th postoperative day. The severity of the postoperative symptoms may be reduced by placing a snug dressing with pressure along the course of the vein segment in the immediate postoperative period. This reduced the amount of blood involved in the thrombosis.

The choice of suture to be placed in the vein is important. The induced thrombophlebitis with a silk suture is of a very mild nature, while that with a chromic suture is severer. However, the risk of infection is higher with a silk suture.

The long-term results are as satisfactory as those of vein stripping. The palpable vein disappears rapidly.

Special care must be taken to avoid contamination of the suture to be placed in the vein. Patients with open lesions on the leg are treated with conservative measures until the skin is healed and all infections of any

nature on the legs have been cleared. It is further believed advisable to soak the suture in saline prior to its use, to remove all excess xylol or other storage agent. When a silk suture is used, routine soaking in a solution of 500,000 units of penicillin in 100 cc. of saline, for three hours, is suggested.

This technique is of value in that it can be done satisfactorily with the area under local anesthesia. It is accompanied by a minimum of trauma and bleeding and is free from the late bleeding sometimes experienced in vein strippings.

It is further advantageous in that it may be done as an outpatient procedure, without the use of a hospital bed.

SUMMARY

Thirty-one instances are presented in which an intraluminal suture was placed in a saphenous vein to cause obliteration of the vessel. A majority of these procedures were done with local anesthesia, supplemented by intravenous meperidine. The immediate morbidity of the procedure is slightly greater, but the long-term results appear to be equal to those of vein stripping.

DISCUSSION

DR. ROBERT NABATOFF, New York: We have been doing complete stripping operations with local anesthesia and have been able to tie off the long saphenous vein at the femoral site, the midthigh branch, and also at the malleolus so that you tie off many of the branches and then just inject the procaine hydrochloride (Novocain) along the vein between incisions. It is not difficult to strip out the entire vein under local anesthesia; this eliminates the need for the suture. We have patients up within one hour, and half go home the same day and half the following day. It works out very well. We have treated several hundred patients now, and results have been very satisfactory. An advantage is that you don't have thrombosed segments in the leg postoperatively.

DR. CHARLES STEINMAN, New York: About two and a half years ago we, at the Marine Hospital on Staten Island, became interested in this technique, and we started to use the intraluminal silk suture on short segments of vein as an introduction and we found that postoperatively most of these patients developed such marked reaction and thrombosis of the vein and complained so much of pain that a week or ten days later, without subsidence of the symptoms, we had to resect these thrombosed veins anyhow.

DR. DAVITT FELDER, St. Paul: Perhaps there is a difference in the patient one sees on Staten Island and one sees in Minnesota. We didn't have to remove any veins and the patients have had an excellent result. We are not proposing that this procedure be used on all patients with varicose veins. We wish this report to be simply an objective one.

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A Comparison of Some Newer Anticoagulants

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For the past two years the hematology service of the Royal Victoria Hospital has been using several different anticoagulants in an attempt to determine which, if any, is the best for routine use and which are most suitable under special conditions. It is the purpose of this paper to describe our experience with the anticoagulants cyclocumarol, 3-(1'-phenylpropyl)-oxycoumarin (Marcumar), and warfarin sodium * and to compare the action of these drugs with each other and with bishydroxycoumarin (Dicoumarol). Experience with cyclocumarol at the Royal Victoria Hospital has been reported elsewhere.†

METHODS

The selection of cases and the application of anticoagulant therapy have been discussed in detail in previous papers.† In brief, the patients utilized for these studies were those referred to the hematology service for anticoagulant therapy, and no special selection was made. The majority of patients suffered from myocardial infarction or venous thrombosis.

In most cases the anticoagulant therapy was controlled by frequent determinations of the prothrombin time by Quick's one-stage method. In a group of experimental cases the concentrations of prothrombin, proconvertin, and combined prothrombin-proconvertin were studied by the methods of Owren and Aas.[3]

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* Supplied by Endo Products, Inc.

† References 1 and 2.

Factor V was determined by the method of Quick and Stefanini.[5] The thromboplastin generation test ‡ was modified only in that barium sulfate-adsorbed plasma was substituted for aluminum hydroxide-adsorbed plasma.

Although there is no known ideal anticoagulant, satisfactory clinical results can be obtained by the careful use of drugs presently available. A good coumarin anticoagulant should have the following properties: (1) a rapid initial action, (2) a predictable response to the initial dose, (3) a consistent response to a given maintenance dose, (4) a prolonged action, (5) minimal hemorrhagic effects, and (6) a rapid and predictable response to vitamin K.

RESULTS

The speed of initial action of three different drugs is compared with that of bishydroxycoumarin in Table 1. The onset of therapeutic effect is herein defined as the time taken to reach a prothrombic complex concentration of 33% or less of normal.

Table 1 shows a progressively increasing speed of action from left to right. With bishydroxycoumarin only 50% of patients achieved a therapeutic effect within 48 hours, as compared with 96% for the patients receiving warfarin.

Eleven patients were given either Marcumar or warfarin intravenously, and though the number of cases is too small to be sta-

TABLE 1.—*Rapidity of Action of Initial Dose*

Onset of Therapeutic Effect	Bis-hydroxy-coumarin 173 Cases	Cyclo-cumarol 142 Cases	Marcumar 40 Cases	Warfarin 31 Cases
Time in Days	%	%	%	%
< 1	8	30.3	40	48.4
< 2	42	52.1	45	48.4
< 3	26	11.3	7.5	0
4 or more	24	6.3	7.5	3.2

‡ References 6 and 7.

TABLE 2.

Drug *	1st Day	2d Day
Bishydroxycoumarin	300	100
Cyclocumarol	150	50
Marcumar	21	9
Warfarin	50-75	0

* All doses in milligrams.

tistically significant, the rapidity of action was essentially the same for the oral and the intravenous route. Not infrequently a situation arises in which the patient is unable to swallow medication or is vomiting or in which small bowel disturbances may make absorption of the drug uncertain. Under these conditions the use of intravenous warfarin or Marcumar is indicated.

An important requirement of any drug is that it should produce a predictable response to the initial dose. In estimating this property it must be remembered that each patient is an individual therapeutic problem, and the dose must always be reduced in conditions in which undue sensitivity is likely to be encountered.[1] The accompanying initial dosage schedule (Table 2) was usually followed for routine use.

Table 3 represents an attempt to analyze the consistency of response to the initial dose and shows the percentage of patients in each series who remained within the therapeutic range from the second to the fifth day, the percentage who failed to reach an adequate level during this period, and the percentage whose prothrombic complex concentration dropped to below 10%.

It can be seen that the more rapid the action of the drug, the more likely it was for the prothrombic complex concentration to drop to a low level. Only a small proportion of the bishydroxycoumarin group decreased to below 10% of normal, but many of the patients took five, six, or more days to reach a therapeutic level. About 30 cases were given biscoumacetate (Tromexan) and bishydroxycoumarin together, and in this group the proportion of patients falling below 10% of normal was comparable with the cyclocumarol and Marcumar groups.

TABLE 3.—*Activity from Second to Fifth Day*

Drug	Inadequate Effect	Therapeutic Range	Below 10%
Bishydroxycoumarin	50	46.2	3.8
Cyclocumarol	17.5	52.5	30
Marcumar	15	45	40
Warfarin	3.8	40	57

Thus it is apparent that in order to achieve very rapid action with this group of drugs one must accept the risk of an excessive decrease in the prothrombic complex concentration. This effect is usually transient and easily controlled. In most cases the omission of the drug for a day or two was sufficient to bring the patient under control. Only rarely did the level drop below 5% of normal and necessitate vitamin K administration.

TABLE 4.—*Average Weekly Dose*

Drug	24-Hr. Onset, Units	Over 4 Days Onset, Units
Bishydroxycoumarin, 50 mg. = 1 unit	7.3	10.6
Cyclocumarol, 25 mg. = 1 unit	6.2	6.8

A consistent response to a given maintenance dose in each case is an important consideration for any anticoagulant, especially in outpatients having relatively infrequent prothrombin determinations. It would be advantageous if maintenance dosage could be estimated early in the course of treatment. To this end an effort was made to correlate speed of onset of initial effect with the maintenance dosage, and the results are shown in Table 4.

Although the maintenance dose of bishydroxycoumarin appears to have been greater in those patients in whom the onset of initial effect was delayed, it was impossible to make any prediction in individual cases. The data from the Marcumar- and warfarin-treated cases are inadequate for such a comparison. As yet there does not seem to be any method of estimating the maintenance dose required in any patient by determining the earliest onset of drug action.

Consistency of response to an anticoagulant is a property that is difficult to demon-

TABLE 5.—*Consistency of Response to Maintenance Therapy*

Drug	Treatment Days	Days Prothrombin Time Too Long	Days Prothrombin Time Too Short	% Days Not in Therapeutic Range (10% to 30%)
Bishydroxycoumarin	2,000	231	61	15
Cyclocumarol	2,000	141	59	10
Marcumar	500	24	16	8

strate concisely, because of the numerous and often variable factors involved in treating a large number of patients. These factors fall into three main groups: first, variations in sensitivity between patients and even in the same patient; second, variations in laboratory procedures, and, third, individual variations in prescribing the anticoagulants. Since the last two factors remained reasonably constant in this series, a comparison of consistency of response to maintenance dose seemed justifiable.

Table 5 is an analysis of cases on maintenance therapy for three weeks or more after the initial effect had been obtained (five days) and gives some idea of the proportion of time that control was unsatisfactory.

It suggests that Marcumar produces the smallest number of days in which the prothrombin level is outside the therapeutic range. In actual practice, however, this was the result of frequent and considerable variation in dosage. It is our impression that cyclocumarol has given the smoothest effect with the least variation in dosage of any of these drugs.

Long-acting anticoagulants are superior to those with a short-lived effect for the following reasons:

1. They do not have to be administered so frequently.

2. They permit smoother effect than drugs with a short action which tend to produce greater swings in prothrombin time from day to day.

3. There is a more gradual decrease in effect after terminating treatment. This minimizes the possibility of overswing, with fresh thrombosis.

All the drugs under consideration, with the exception of bishydroxycoumarin, are long-acting. They require 7 to 14 days to return to normal after therapy is stopped, with an average of 8 to 10 days. The duration of effect of bishydroxycoumarin is somewhat shorter (four days).

When large numbers of persons are treated with anticoagulants, it is inevitable that there will be a few cases with hemorrhagic complications, especially in patients who have recently undergone surgery.

The complications encountered in this series are shown in Table 6.

Bleeding occurred in 4% of the total series, and in about one-third of these the prothrombic complex concentration was below the therapeutic range.

In six cases the bleeding was serious. Five of these occurred in the bishydroxycoumarin series and one in the cyclocumarol. In the remaining 15 cases of bleeding on all forms of therapy, the concentration was minor in character and was rapidly brought under control. Errors in management were probably responsible for the two most serious cases.

The response to vitamin K_1 emulsion given intravenously was satisfactory with all the drugs used in this series. Only small doses, in the order of 2 mg., should be given when it is desired to maintain a patient on anticoagulants. Larger doses cause loss of therapeutic effect and resistance to further therapy. A small dose may be repeated if necessary.

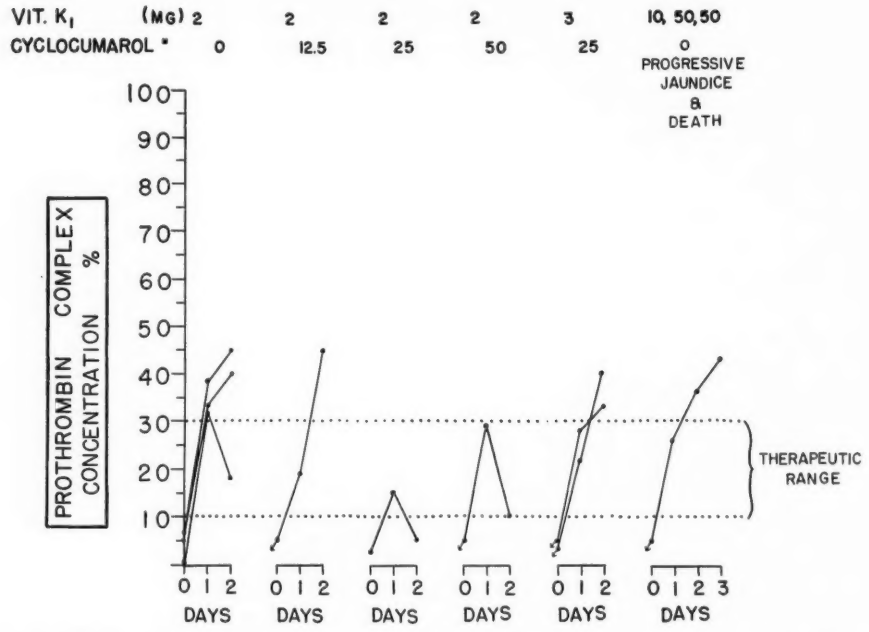
Figures 1 and 2 depict the effect of these small doses on patients with excessive anticoagulant effect from the coumarin drugs.

TABLE 6.—*Hemorrhagic Complications*

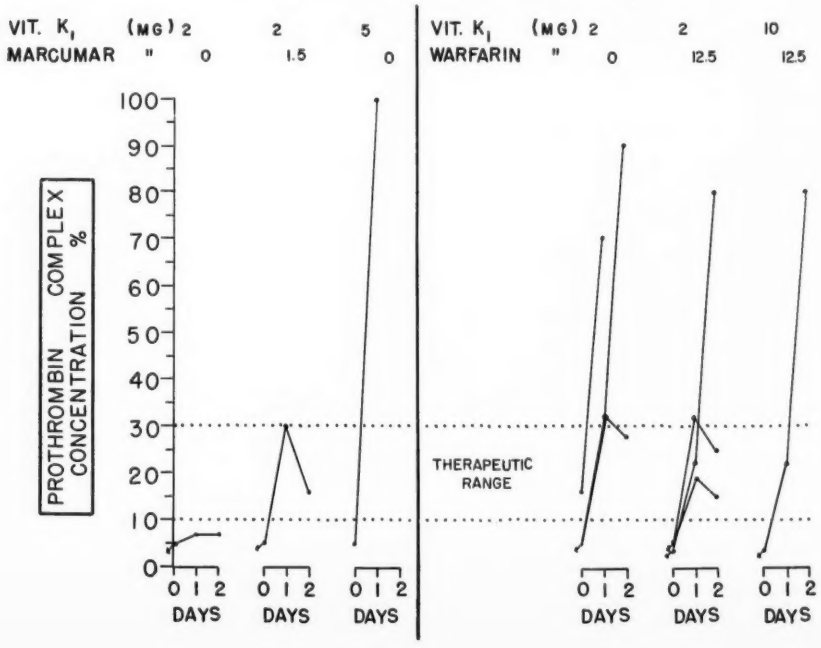
Drug	Total No. of Cases	No. with Bleeding	Prothrombin Complex Concentration >10%	Prothrombin Complex Concentration <10%	% of Hemorrhages
Bishydroxycoumarin	275	15	10	5	5.4
Cyclocumarol	180	4	2	2	2.2
Marcumar	37	0	..	..	...
Warfarin	31	2	1*	1	...

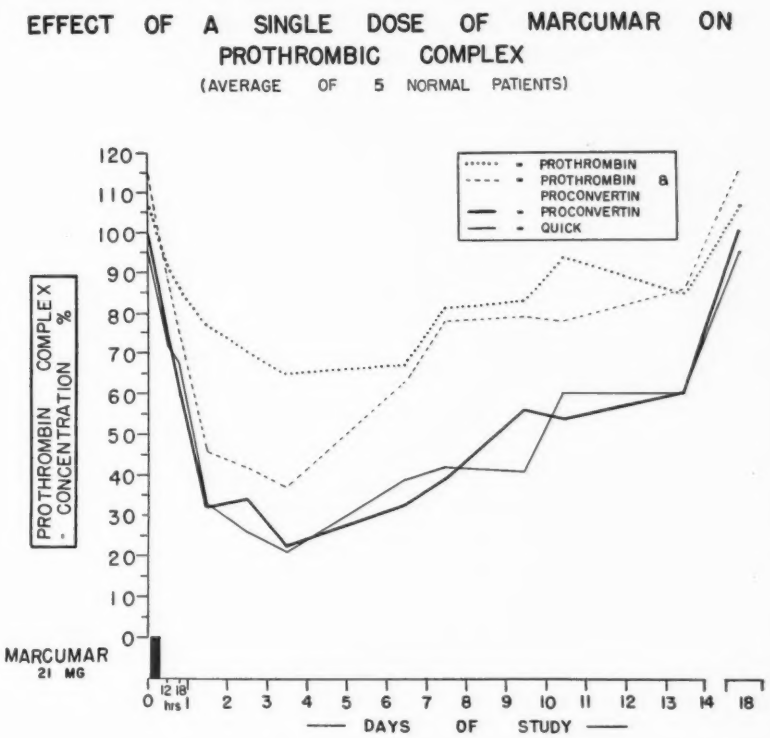
* On Heparin C.T. 66'

TREATMENT OF EXCESSIVE CYCLOCUMAROL EFFECT WITH VITAMIN K_1



TREATMENT OF EXCESSIVE MARCUMAR AND WARFARIN EFFECT WITH VITAMIN K_1





It is desirable to continue anticoagulant therapy on the day after administration of vitamin K_1 if the prothrombic complex concentration rises above the therapeutic range. This is especially illustrated by a patient receiving Marcumar who was given 5 mg., with return of prothrombin time to normal in the absence of continued Marcumar administration. Larger doses may be required in the presence of liver damage, as is illustrated by the patient on cyclocumarol therapy who developed progressive jaundice and died.

LABORATORY CONTROL

Patients receiving anticoagulant therapy may develop hemorrhagic complications when the prothrombic activity is within or above the so-called therapeutic range, and frequently there is no bleeding when the prothrombic activity is well below the therapeutic range. This has led to questioning of Quick's prothrombin method in the control of anticoagulants, and it has been stated § that improved methods for assessment of prothrombin and/or proconvertin provide better control of therapy.

In order to compare these methods, the several fractions of the prothrombic complex were studied serially in patients and in normal subjects receiving coumarin-type anticoagulants. The results will be reported in detail in another paper. Figure 3 is representative of our findings. For practical purposes Quick's prothrombin time is as satisfactory as any of the three more complicated methods of Owren. However, when the test cannot be completed within a few hours of drawing the blood, Owren's proconvertin method is suitable, whereas Quick's method is not accurate under these circumstances. Inasmuch as the prothrombic complex concentration of a plasma sample is lower by

§ References 3 and 4.

Quick's method than by Owren's P and P method, adoption of the latter would necessitate clinical reevaluation of the usually accepted therapeutic range of 10 to 30%.

Factor V was not affected significantly by any of these anticoagulants, and no consistent abnormality was found with the thromboplastin generation test. Consequently we have not found this test to be of practical help for the routine estimation of deficiencies of Factor VII, of Koller's Factor X,‖ or of PTC [13] in patients receiving these anticoagulants.

CONCLUSIONS

1. Cyclocoumarol, 3-(1′-phenylpropyl)-oxycoumarin (Marcumar), and warfarin sodium are useful anticoagulants. Of the three, cyclocoumarol has proved the most satisfactory in our hands and is also superior to the shorter-acting coumarin anticoagulants.

2. Marcumar and warfarin given intravenously are satisfactory when oral therapy is difficult.

3. If intravenous administration of vitamin K is required and it is desired to maintain the patient on anticoagulants, dosage in the order of 2.0 mg. should usually be given.

4. The Quick one-stage prothrombin test or one of its modifications provides as satisfactory a method of laboratory control as is yet available, except when examination must be delayed several or more hours, in which case Owren's proconvertin test is more accurate.

DISCUSSION

DR. MARTIN M. FISHER, New York: I believe these Montreal doctors should be congratulated on an excellent paper. We have all been attempting to find the ideal anticoagulant drug, particularly for the use in ambulatory anticoagulant therapy where we don't have to worry each day about prothrombin times. This cyclocumarol sounds like the drug which has potential. Last year and the year before we reported on the use of phenindione (Hedulin), which originated in Canada also. There was a predictability in that, with an initial dose of 400 or 500 mg., 70% of the patients achieved a therapeutic level in 24 hours. We were able to maintain patients thereafter with doses of 50 to 150 mg., and the predictability or maintenance was adequate in all those cases. Regarding hemorrhage, we found little or no hemorrhage in our cases.

Occasionally when surgeons have patients with thrombophlebitis or recurrent thromboembolism, they would like to consider conservative management with anticoagulants first, before consideration of ligation. A quick-acting anticoagulant that can be quickly reversed, such as cyclocumarol and phenindione, is well indicated. Phytonadione (vitamin K_1) oxide is an excellent aid in lessening the fear of the hemorrhage from anticoagulant drugs. We find in our studies that with phytonadione oxide we could reduce the prothrombin time to therapeutic levels, out of dangerous range, within four hours. Occasionally we see a rebound, however.

DR. OLWIN, Chicago: I believe we are at the point now where we can choose anticoagulants to fit the situation. If we want long-term therapy with a possible rapid recovery or if we want short-term therapy with a possible rapid recovery or long-term therapy with slower recovery and with perhaps more uniform control, these objectives can be reached according to the anticoagulant we select. I believe the chief difficulty is the factor of control. As you know, anticoagulants are still used warily or not at all by many clinics; these institutions have had difficulty with control and in some instances disastrous results, such as severe hemorrhage or recurrent thromboembolism. I believe that as soon as we get a satisfactory simple method for their control, anticoagulants will be more readily accepted throughout the medical world. They are safe. We have some patients who have been on anticoagulant treatment now for seven years. They come in or send their blood in every two weeks for prothrombin determinations, some of them sending samples from as far as Mexico, Jamaica, and Hawaii.

We recently have studied seven thromboplastin preparations, five of them being commercially available and two of which we have made in our own laboratory. We found that in the one-stage test, using the curves that were set up for the individual thromboplastin reagents and testing those reagents on the same plasmas, there were prothrombin percentage values varying all the way from 10% to 100%. It is little wonder that many people have rejected anticoagulants. You can see how results from different clinics all over the world are not comparable. The two-stage test, on the other hand, has in our laboratory given very satisfactory results. It is, however, an involved test and is not practical for most clinical purposes. So I believe that until we get a satisfactory test that is very simple we will

‖ References 8 to 12.

not have uniform opinion on anticoagulants. Such a test may be in the offing. It may be the first chemical approach to prothrombin estimation and has to do with a synthetic thrombin substrate called tosyl-arginine-methyl-ester (TAME). It offers the possibility of a simple, uniform control of prothrombin, and I hope that within the next few years it will be available to all clinicians.

DR. JOSEPH C. LUKE, Montreal, Canada: May I give the surgical viewpoint to this excellent paper from the Royal Victoria Hospital. I have the pleasure of working with Drs. Lowenstein and Brunton and can truthfully say that a well-run hematology department can do more for the patient with venous thrombosis and embolism than can the surgeon. In the past three years I have not ligated a deep vein for thrombembolism, as this operation has become unnecessary if good anticoagulant treatment is available. I have never ligated a vena cava, for the same reason, and believe that all surgery in thromboembolism is unwarranted when good medical management exists. This is one instance where a previous field of surgery has passed over to medical hands.

DR. LAUDER BRUNTON, Montreal, Canada: We believe that long-acting drugs are definitely preferable to short-acting drugs under all circumstances because of what has been said about phytonadione. With this drug the anticoagulant effect can be stopped almost instantaneously. With the short-acting drugs it is really impossible to prevent swings in the prothrombin concentration. Quite marked swings may occur from day to day and even on the same day as the prothrombin test. We feel cyclocumarol is a very good drug. It has just been neglected and should be brought to people's notice. We admit there is no method in determining who is going to bleed because there is no correlation or very little correlation between the low prothrombin concentration and hemorrhage. It is fair to say that in our series, the only two cases of serious bleeding were due to mismanagement.

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Excision and Drainage for Infections of the Foot with Gangrene in the Diabetic

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and
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Gangrenous lesions of the foot in the diabetic patient may be classified into three groups,[1] clinical differentiation among which is important in prognosis: (*a*) Gangrene due to arterial insufficiency with minimal or no associated infection. This type is almost always acral in distribution and "dry" in appearance. (*b*) Gangrene of local nature, secondary to the destructive action of infection. The association of this form of necrosis with diabetes mellitus is frequent. (*c*) Gangrene of combined etiology, with elements of vascular impairment and infection intermixed, a group most difficult to evaluate.

Emphasis will be given in this report to instances of gangrene secondary mainly to infection or to infection combined with varying degrees of major arterial disease. Such "septic necrosis" can occur at any of the following sites in the foot and usually follows relatively minor trauma to the skin.

(1) In the toes, about the nails, or in relation to "corns," "bunions," or hair-follicle infections.

(2) In the webs between the toes, most commonly after maceration of the skin by excessive moisture with or without dermatophytosis.

(3) On the dorsum of the foot, following abrasion or direct trauma.

(4) Over the plantar aspect of the metatarsal heads, usually in association with diabetic peripheral neuropathy and usually leading to chronic ulceration.

(5) In the heel area, often originating in thick, dry, fissured skin and leading eventually to a blackened, plaque-like eschar or an ulcer extending to the os calcis.

The term "gangrene" cannot be limited to obvious areas of skin blackening but must also be applied to sloughs found beneath the surface. Great confusion is engendered when the element of gangrene which is secondary to infection is not recognized as such but is considered the result of vascular insufficiency. Many of these patients are referred for major amputation. However, good results from conservative surgical excisions are often obtained in this group.

The susceptibility of the diabetic to infection, particularly when the diabetes is poorly controlled, is well documented. In the foot these infections may lead to obviously recognizable cellulitis and abscesses requiring incision and drainage. They can also produce necrosis of tissue, visible on the surface as blackening of the skin. The deeper layers may reveal more extensive necrosis of fat, fascia, tendon, and muscle, with suppuration involving the spaces between those structures. The amount of free pus which can be evacuated by drainage procedures may be minimal, and simple incision of these areas has not proved adequate to cope with the clinical situations we have encountered.

In 1939, before the antibiotic era, Zierold [2] employed early excision of all necrotic tissue and unroofing of all infected areas in the foot, without attempting to save important structures. This was usually performed as

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Fig. 1.—*A*, gangrene of third and fourth toes with cellulitis and abscess involving dorsal subaponeurotic space, distal portion of deep plantar space, and lateral two web spaces. *B* and *C*, after preliminary amputation of necrotic toes with unroofing and débridement of deep areas of suppuration in foot. *D* and *E*, after secondary transmetatarsal amputation. Second intention healing permitted. *F*, final result. (Reproduced from Kodachrome transparencies.)

a preliminary to major amputation, which he then carried out, with a considerable lowering of the mortality rate. With the availability of antibiotics such excisions can possibly become definitive therapeutic procedures, conserving limb as well as life.

It has been our aim in the treatment of septic gangrene in the diabetic to attack areas of combined infection and necrosis early and by radical excision down to healthy-appearing tissue. Antidiabetic therapy is intensively administered as a preliminary to surgery to achieve some measure of control over glycosuria, ketonuria, and dehydration. The local lesion is usually excised or unroofed as early as possible in the knowledge that it may itself be contributing to difficulty in controlling the diabetes and to provide adequate drainage for otherwise "locked-in" areas of necrosis and suppuration. The resulting wounds are treated by delayed closure or are permitted to heal by second intention whenever infected or sloughing tissue cannot be excluded from the operative field. Pinch grafting is employed to cover granulating areas where indicated.

In many cases there is associated vascular impairment of varying degree. When this

is marked, the extent and distribution of necrosis will preclude attempts at conservative therapy and major amputation may be required primarily. When the degree of associated arterial insufficiency is moderate, the fate of the limb after the excision and drainage procedure hangs in the balance and varies with the amount of residual blood supply. Favorable signs consist of warming of the foot in response to the infection and, most important, the encountering of reasonably good bleeding at operation. The presence of palpable dorsalis pedis or posterior tibial pulses are fairly certain signs for a favorable outcome.

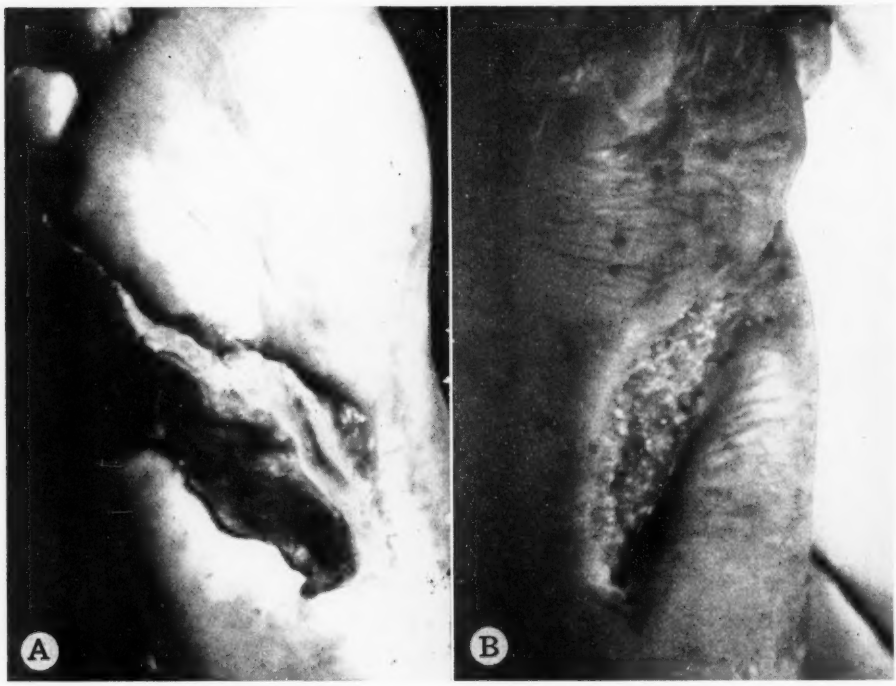

Fig. 2.—*A*, full-thickness plaque of cutaneous gangrene in sole of foot. *B*, after excision and subsequent pinch-grafting. (Reproduced from Kodachrome transparencies.)

SURGICAL TECHNIQUES

1. *Lesions of the Toes.*—In lesions of the central toes transmetatarsal amputation is most commonly practiced, the surgeon employing the technique of McKittrick and associates,* and practising primary or delayed closure or permitting second intention healing when indicated † (Fig. 1).

In cases of first- or fifth-toe involvement isolated metatarsophalangeal resection has usually been performed. This has provided a useful foot with somewhat more stability than the full forefoot amputation.

When second intention healing is awaited, the skin edges are loosely held in apposition by the adhesive action of petrolatum (Vaseline) gauze and the pressure of a superimposed bulky dressing, thereby securing earlier coaptation of wound edges.

With lesions of the toes extension into the associated web spaces and distal foot is common. In such instances these spaces are unroofed, the deep sloughs are débrided, and a secondary transmetatarsal amputation is

* References 3, 4, 5, and 6.

† References 7 and 8.

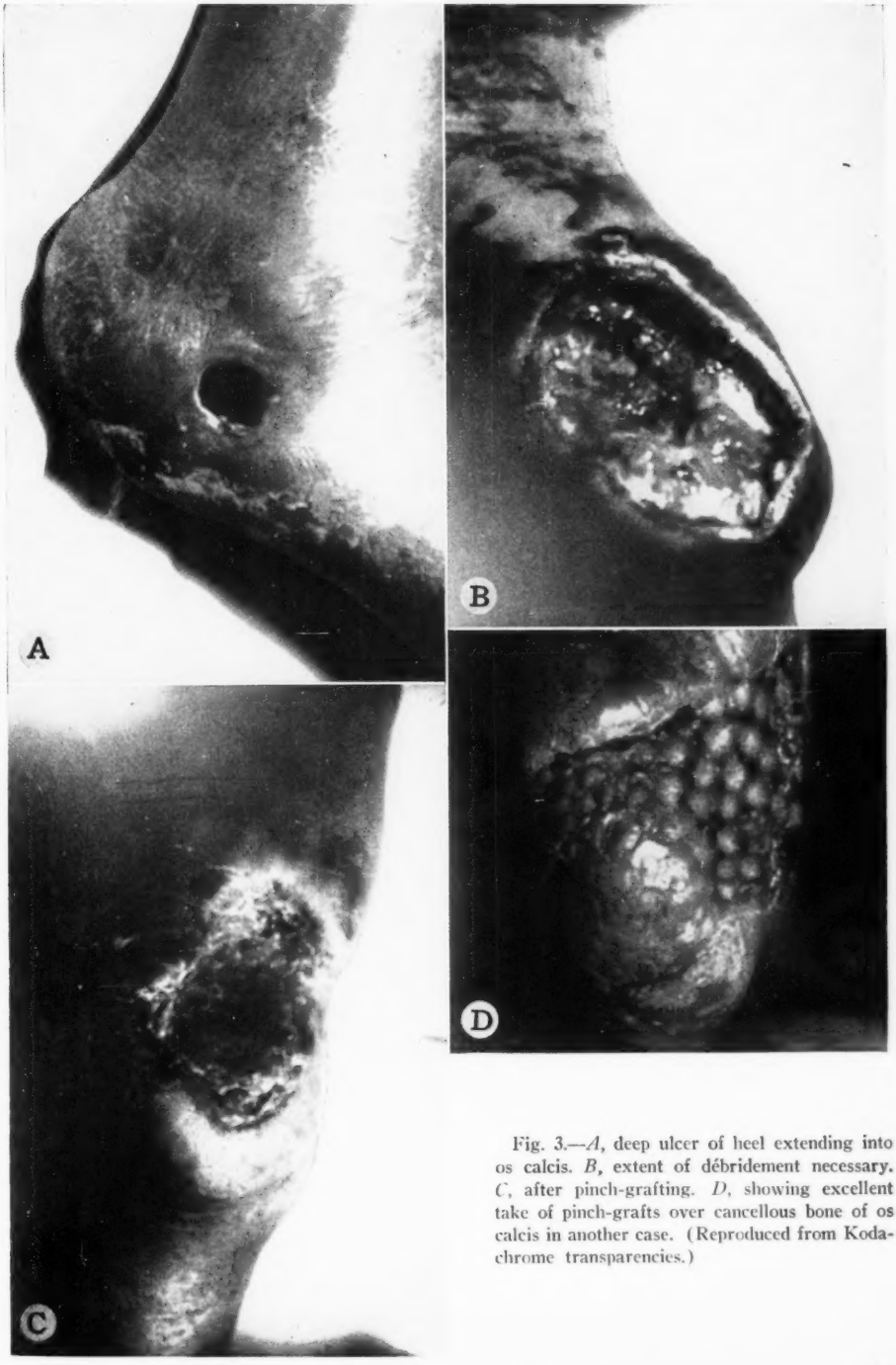

Fig. 3.—*A*, deep ulcer of heel extending into os calcis. *B*, extent of débridement necessary. *C*, after pinch-grafting. *D*, showing excellent take of pinch-grafts over cancellous bone of os calcis in another case. (Reproduced from Kodachrome transparencies.)

performed at a later date, after clean granulations have formed.

2. *Lesions of the Sole.*—Localized cutaneous gangrene is treated by excision, with delayed pinch grafting (Figs. 2*A* and *B*). The trophic ulcer present in the sole over the metatarsal heads and associated with diabetic peripheral neuropathy has been similarly excised either in limited fashion or with associated metatarsophalangeal, or forefoot, resection.‡

3. *Gangrene of the Heel.*—Gangrene of the heel is commonly seen either as an isolated lesion or in association with other lesions of the foot in the diabetic. It may present itself either as a superficial plaque of blackened skin or as an area of suppuration and necrosis extending down through the underlying dense, loculated fat to or into the os calcis.

The plaque-like cutaneous lesions have been successfully treated by excision with or without subsequent grafting.§ The deeper infections have little free pus and cannot usually be drained by simple incision. Instead, radical excision down to healthy tissue is required, often involving removal of most of the heel pad (Fig. 3). Where the os calcis is exposed, as it has been in three cases, it has been our practice to chisel away all presenting cortical bone, leaving a flat cancellous bony surface which, by virtue of its rich capillary supply, provides an adequate bed for the application of pinch grafts (Figure 3*D*). We have usually made no attempt to provide weight-bearing skin for the heel area in elderly persons and most have been able to get about fairly well, without graft breakdown, by directing their weight to the intact forefoot during ambulation.

Since 1948, fifty-eight lower extremities in diabetics were treated for infection and associated gangrene. Of this group 24 required primary major amputation and 3 had simple toe amputation. Of the remaining 31 limbs 17 responded favorably to local excisional procedures with conservation of limb function. In 14 limbs local surgery was followed by major amputation (Table).

‡ References 3 and 4.

§ References 9 and 10.

COMMENT

Diabetes mellitus is an additional handicap to the patient with vascular impairment in the lower extremities. However, in a limb presenting a gangrenous lesion the prognosis may be paradoxically better for the diabetic than for the nondiabetic. In purely "vascular" gangrene the necrosis is the direct result of arterial disease, which can be influenced only slightly, but in the diabetic with gangrene the possibility always exists that much of the necrosis may be secondary to infection which can be successfully treated by antibiotics and excisional surgery.

Operative Procedures and Results

Type of Operation	No. Performed	Failures
Closed transmetatarsal amputation	9	4
Open transmetatarsal amputation	8	5
Isolated metatarsophalangeal resection	7	3
Excisions in heel area	7	3
Excision of trophic ulcers	3	0
Excision of gangrenous plaque in sole	1	0
Total	35	15
Successful limb conservation (no prosthesis required)		17 limbs
Unsuccessful cases (subsequent major amputation)		14 limbs

Two-thirds of patients were between 60 and 80 yr. of age. Palpable foot or ankle pulses present in only 7 of 31 limbs.

In some instances the issue was precipitated by local excision, the blood supply proved inadequate for healing, and major amputation was required. In others early excision and drainage were rewarded by fairly prompt resolution of the issue in favor of limb conservation. The operation of excision and drainage may thus serve as a definitive test of blood supply, the preoperative estimation of which is so often a combination of clinical experience and guesswork.

There are other factors besides blood supply which may determine the outcome in such cases. The nature of the infecting organism and its responsiveness to antibiotics is important even in the presence of fairly good blood supply. One of our patients succumbed

to a Proteus sepsis resistant to antibiotics. The presence of complicating degenerative states, particularly the Kimmelstiel-Wilson syndrome, may also lower the ability of the patient to combat both the metabolic disturbance and the local lesion.

SUMMARY

Gangrene associated with infection is a special problem in the foot of the diabetic patient. The principle of "excision and drainage" has been employed successfully in the treatment of such septic necrosis and has permitted preservation of a useful foot remnant.

The most commonly performed, formal procedures are transmetatarsal amputation, isolated metatarsophalangeal resection, and excision of the heel.

Cases in which infection complicates an underlying arterial insufficiency are more difficult to evaluate, and in these the prognosis depends on the severity of the vascular disease. The "excision and drainage" procedure seems to serve as an adequate test in this group, leading usually to limb conservation when the blood supply is adequate for healing and to major amputation when it is not. The amount of bleeding noted at the time of surgery remains an important prognostic sign in this regard.

The functions of the human foot are limited, being mainly those of weight bearing and locomotion. Much tissue can therefore be sacrificed to infection and gangrene, and to the surgeon's knife, without an inordinate crippling of the weight-bearing function of the limb and the patient's ability to get about.

DISCUSSION

DR. RICHARD WARREN, Brookline, Mass.: I rise only to congratulate Dr. Rosenberg and support him wholeheartedly in the paper he has presented. It is extremely important to emphasize the point he has just made that these patients with the good circulation should be differentiated from the patients with poor circulation and blackness of skin or toes doesn't necessarily mean a limb which has had a major occlusion of the circulation. An additional point might be made. With our house staff we have so much difficulty in conveying an understanding of this point that we have told them that a patient suspected of being in this category should have at least a preliminary exploration with sterile forceps and scissors of the necrotic area as part of the admission physical examination. Most of them have diminished sensation, if not complete absence of pain sensitivity, and much can be done on the ward in appraising the depth of the lesion or the extent to which it is an "iceberg," as Dr. Rosenberg so well puts it. One can also discover from the degree of bleeding what the circulation is like.

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Metabolic Derangements Imperiling the Perforated Ulcer Patient

III. Derangements and Shifts of Sodium and Chloride

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INTRODUCTION

Cellular function is affected by the composition and concentration of electrolytes within the cells, and their concentrations, in turn, are governed by a complicated equilibrium with the electrolytes in the fluid bathing the cells. A disease state or a therapy influencing the extracellular phase to the extent of altering the intracellular electrolytes may be damaging to cell function. In the first paper of this series, concerned with the fluid shifts occurring after ulcer perforation, observations are described which might be explained by penetration of extracellular electrolytes across cell barriers.[1] Substantiation or refutation of this possibility in the patient with a perforated peptic ulcer should alter our therapy.

Post-traumatic salt retention has received much attention in the literature,* and simultaneous drops in serum sodium and chloride concentrations have been described. In 1944, Coller and his associates described a fall of the chloride level associated with chloride retention.[5] A subsequent study of severe burns in this hospital afforded an opportunity to observe a similar lowering of the sodium level during a period of post-traumatic sodium retention.[11] The paradoxical nature of these observations is mentioned by Coller and has been emphasized more recently by Moore,† who finds the paradox to be a characteristic postoperative phenomenon. To explain this extraordinary situation, Moore has suggested that sodium shifts into muscle cells or bone after trauma.† In these studies of patients with perforated peptic ulcers, we have found that the apparent paradox of falling sodium and chloride concentrations during sodium and chloride retention can be simply explained without invoking the concept of intracellular accumulation of these extracellular electrolytes.

PLAN OF STUDY

The plan of study of the extracellular electrolytes was restricted to observation of the changes in the serum concentrations and balances of sodium and chloride ions. They are quantitatively the dominant ions of the extracellular fluid.‡ No attempt was made to alter their serum concentrations or their balances by controlling the intakes.

Sodium and chloride administration was at the discretion of the house staff and varied considerably from patient to patient. All received salt solution

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From the Department of Surgery, Harvard Medical School, and the Surgical Services, Massachusetts General Hospital.

* References 2 through 11.

† References 12 and 13.

‡ In excluding the other extracellular electrolytes we do not wish to deny their importance to bodily function.

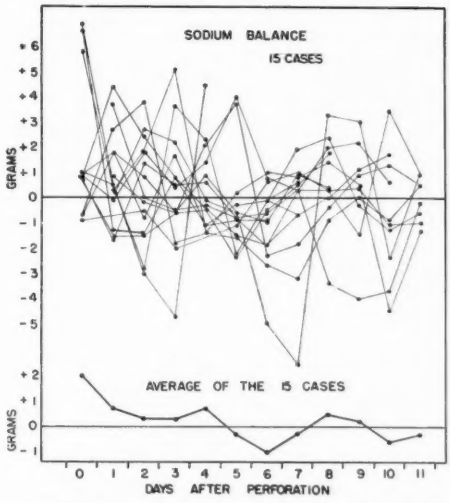


Chart 1.—The sodium balance in 15 surgically treated cases. Twelve of the fifteen retained sodium in the initial days. In the case treated without operation the balance followed the same trends.

as part of the fluid therapy for dehydration, and additional amounts of sodium and chloride were administered in some cases as a part of infused whole blood, amino acid hydrolysates, or potassium salt solutions (see Table 1, Paper II).[14] Neither the time of resumption of salt administration by mouth nor the quantity by this route was standardized.

The main features of the investigative routine were described in the first paper of the series.[1] Intake data were derived from careful volumetric measurements or weights, as described in the second paper.[14] Urine, stools, gastric drainage, and peritoneal fluid were analyzed for sodium and chloride.

Methods.—Sodium was measured by the Perkin-Elmer flame photometer, the chloride by the standard chemical procedure.[15]

SODIUM OBSERVATIONS

Sodium studies were carried out in 23 cases. The concentration of sodium in the serum was measured with sufficient frequency in 19 to determine the trend in each. Sodium balance data were obtained for 15 of the 19 cases. Occasional serum sodium determinations were made in four additional cases.

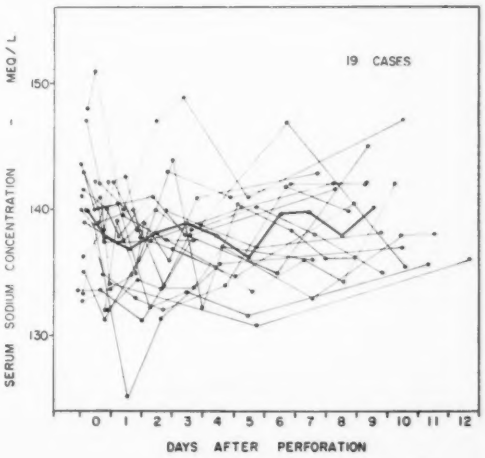
Individual variations in sodium balance and serum sodium concentration were wide (Charts 1 and 2), but trends can be delineated.

During the day of perforation and the first two postoperative days, sodium was retained by patients on high and low sodium intakes alike. In the majority this retention was accompanied by a fall in serum sodium concentration, the so-called "sodium paradox." On the third and fourth days the average patient continued to retain sodium, and the serum sodium level rose. Then, a reversal of sodium balance took place. As the previously retained sodium was eliminated, the serum sodium concentration rose in six patients.§ Five patients, on the other hand, showed a falling concentration at this time. Blood samples were not taken with sufficient frequency in the remaining cases to determine the presence or absence of this second paradox.

During the second postoperative week, the sodium balances fluctuated with sodium intake, while the serum sodium level tended to return to normal. Secondary sodium retention occurred in the "high"-intake cases (greater than 75 mEq. per day), whereas the cumulative sodium balance became nega-

§ This second paradox has been described by Moore.[12]

Chart 2.—The serum sodium concentration in 19 cases. A fall after admission occurred in 15 patients and was associated with sodium retention in 12, the so-called "sodium paradox." The heavy line indicates the average sodium concentrations.



tive in those receiving little or no supplementary sodium.

The details of these observations and descriptions of the exceptional cases which failed to follow the general trends are presented in the subsequent paragraphs.

A. Falling Serum Sodium Concentration During Sodium Retention: The So-Called Paradox

During the early postoperative period, a fall in serum sodium concentration coincided

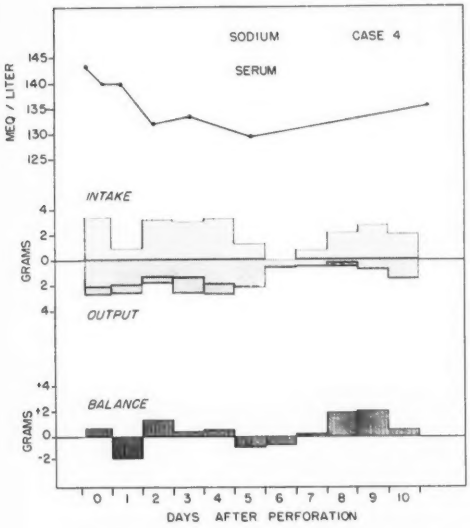


Chart 3 (Case 4).—The initial sodium "paradox." The serum sodium concentration fell during the phase of sodium retention. In this patient the expansion of the thiocyanate space by the 55th hour after perforation was 6.4 liters and the positive fluid balance 2.0 liters. The volume of edema necessary to account for the missing sodium is calculated to be 1.5 liters.

with sodium retention in 13 cases (Charts 1 and 2). In the average case the sodium concentration dropped 5.4 mEq. to reach the lowest level on the second postoperative day. Cumulative sodium retention during the same period (uncorrected for sweat losses) averaged 91 mEq. The balance and serum concentrations of a typical case are shown in Chart 3.

1. *The Early Sodium Retention.*—On the day of perforation sodium intakes were high, and sodium was retained in all but 3 of the 15 surgically treated cases (Chart 1). Retention averaged 6 mEq. per hour (33 gm/24 hr.). One of the exceptions lost only 1 mEq. an hour for five hours on a sodium-free intake. The other two showed negative balances of 1 and 3 mEq., the first for 20 hours and the second for 8½ hours, on hourly sodium intakes of 7.4 and 6.5 mEq., respectively. The case without operation followed the trend of the majority.

Sodium retention persisted during the first three postoperative days in 12 of the 15 cases. In four it was persistently positive, and in eight, although output at times surpassed intake, the average balance for the three days was positive. Intakes during this period continued slightly higher than the average for the postoperative period (156 mEq., 161 mEq., and 169 mEq. on Days 1, 2, and 3). Despite removal of 35 to 43 mEq. of sodium per day by nasogastric suction, total sodium outputs (129, 135, and 143 mEq.) were lower than on the subsequent days. The amount of sodium lost through perspiration was not determined.‖ Urinary losses are described below.

Cumulative sodium balances have been calculated for 11 of the patients who had relatively uncomplicated postoperative courses. Ten of these showed a peak in sodium retention on the second to fourth days, with an average maximum value of 183 mEq., the range being 39 to 365 mEq.¶ The peak in the 11th case was reached on the fifth postoperative day.

2. *Exaggeration of Early Sodium Retention by High Sodium Intake.*—During the

‖ Conn has shown that the concentration of sodium in sweat diminishes after operation.[16] From normal concentrations of 15 to 60 mEq/L. there may be a 50% fall. Hardy and Ravdin find that the volume of sweat decreases postoperatively.[17] Even if our patients had lost as much as 500 cc. of sweat a day and had maintained a normal sweat sodium concentration, they would not have gone into negative balance in the early postoperative period.

¶ Had the sweat sodium been taken into account, these figures would have been reduced. This same consideration applies to the subsequent discussions of sodium balance.

day of perforation and the first day or two postoperatively, the patients on high intakes retained significantly larger amounts of sodium than the low-intake cases (Table). On the next two days, however, the sodium elimination gained pace and the high-intake cases showed a larger negative balance than the low-intake group. At this time the difference in balance between the high- and the low-intake groups was not significant. The balances of the two groups are shown in Charts 4*A* and *B*.

3. *Early Changes in Serum Sodium Concentration.*—The serum sodium concentration, measured on admission in 19 cases, was within the normal range in 12 patients (136-145 mEq/L.), elevated in 2 (147 and 148 mEq/L.), and subnormal in 5 (133-135 mEq/L.) as shown in Chart 2. In all but four of these cases the sodium level subsequently fell (range: 1.5-15 mEq/L.).

Of the 15 patients showing a drop in serum sodium after admission, 13 exhibited the apparently paradoxical sodium retention. No sodium balance study was made in the 14th case. In the 15th a persistent negative sodium balance was observed.

4. *Preexisting Hyponatremia.*—The presence of one patient in the hospital for medical treatment of his ulcer prior to perforation offered us the unusual opportunity to observe the serum sodium concentration while penetration of an ulcer through the duodenal wall was in progress. Serum concentrations five and two days before perforation were 128.4 and 133.6 mEq/L., respectively. Of the five other patients who were hyponatremic on admission, one was admitted 12 hours after perforation, but in the other four there was no delay between perforation and admission. It is possible in these cases that the low sodium concenrtation may also have existed for some time before perforation.

5. *Initial Hypernatremia in a Patient Subsequently Developing Complications.*—The patient with hypopotassemia, possible water overloading, and a wound dehiscence, described in the second paper of this series,[14] was one of the two exhibiting hypernatremia on admission (Case 23: 148 mEq. of sodium per liter). His sodium concentration rose to 151 mEq. 11 hours after perforation, although no sodium was given. Subsequently, it followed the trend of the majority, falling to 139.5 mEq/L. on the second postoperative day in conjunction with a positive sodium balance. Dehiscence and surgical closure took place on the fifth day. No visible evidence of difficulty in wound healing was observed in the other patient with initial hypernatremia.

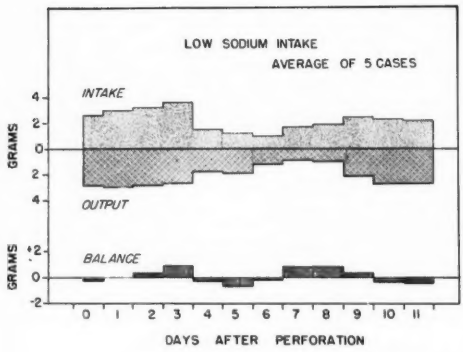
Total Sodium Excretion of Patients with Perforated Ulcers on High and Low Sodium Intakes (Data from This Series)

No. of Patients	Period of Study	Sodium Intake	Average Sodium Intake per Day, Gm.	Average Sodium Output per Day,* Gm.	Average Sodium Balance, Gm.
5	First 4 postoperative days	Low	2.8	2.7	+0.1
5	First 4 postoperative days	High	4.6	3.7	+0.8
4	5th-7th postoperative days	Low	1.2	1.4	−0.2
5	5th-7th postoperative days	High	3.4	4.3	−0.9

* Exclusive of sweat sodium losses.

B. Reversal of Early Trends: Sodium Elimination and Rising Serum Sodium Concentration

Variations occurred from patient to patient in the time elapsing before the fall in serum sodium concentration was replaced by a rise or the sodium retention gave way to sodium elimination. In five the rise in serum concentration occurred while sodium retention persisted. In six it coincided with negative balance, a secondary "paradox." Two patients, included in the numbers just given, showed a rise in sodium concentration during both phases of sodium balance. For the remainder of the cases, data are not



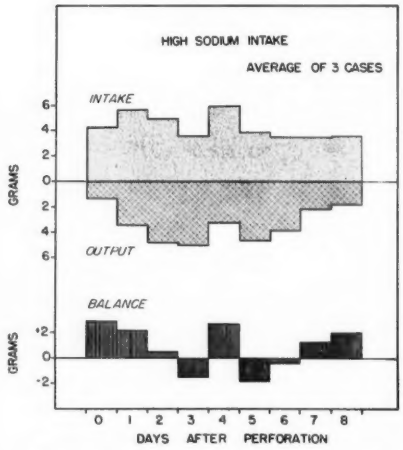


Chart 4*A*.—Exaggeration of sodium retention by high sodium intakes. Average intake, output, and balance of five patients on low sodium intakes, showing a mildly positive cumulative sodium balance at the end of the third postoperative day followed by a trend to negativity.

Chart 4*B*.—Exaggeration of sodium retention by high sodium intakes. Average intake, output, and balance of three patients on high sodium intakes, showing a strongly positive cumulative balance in the initial days. On the fourth day, when the majority of the patients were eliminating sodium previously retained, a high sodium intake caused further retention in these three cases.

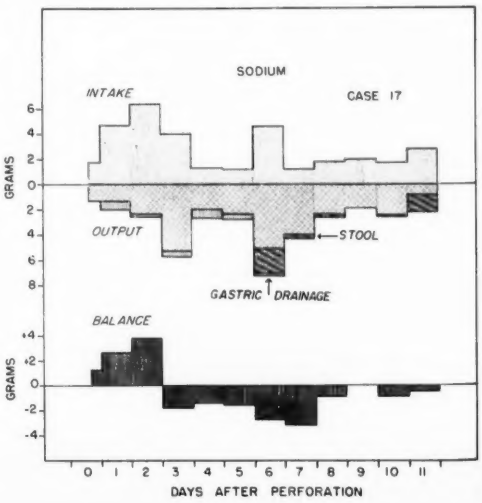
available to show the time relation of the serum changes to the continued retention or subsequent elimination of sodium.

1. *Elimination of the Retained Sodium.*—On the fourth day after perforation the daily sodium balances of half of the patients were negative, and by the following day all but three of the surgically treated cases had begun to excrete sodium in excess of their intakes. The duration of this period of sodium elimination varied from one to six days, the average being three (Chart 1). In most of the cases negative balance appeared to persist only long enough to eliminate the sodium previously retained, but in five patients receiving less than 7 gm. of sodium a day during the second week sodium elimination continued to the extent of an eventual cumulative deficit. A typical case of late sodium depletion is shown in Chart 5.

The case not operated on followed the trend of the average surgically treated case at first, exhibiting mild early sodium retention (less than 1 gm.). Subsequently, he developed a 9 gm. deficit, despite a sodium intake exceeded by that of only 1 other patient of the 15 under study.

2. *Delayed Sodium Elimination in Patients Receiving "High" Sodium Intakes.*—The patients on sodium intakes above 3 gm. a day retained sodium or showed only a small deficit on the fourth and fifth postoperative days, while those on lower intakes passed into pronounced negative balance. The

Chart 5 (Case 17).—Progression of sodium elimination into cumulative sodium deficit in a patient on a low sodium intake. Patients receiving less than 7 gm. of sodium a day during the second week after perforation developed a sodium deficit comparable with the deficit in this case.



sodium balances of these "high"-intake cases were significantly more positive than those of the low-intake cases despite their larger sodium excretions.

3. *Rise in Serum Sodium Concentration.*—A rise in serum sodium concentration succeeded the initial fall in 15 patients during the first postoperative week (Chart 2). In 12 this rise had occurred by the third postoperative day. In eight the rise was transient.

C. Cumulative Sodium Deficits in the Absence of Late Sodium Therapy

The sodium balances of seven patients with an uncomplicated postoperative course were followed through the 10th day. Two late trends were observed. Four patients with sodium intakes below 75 mEq. (1.7 gm.) per day during the first half of the second week went into negative balance again, developing a sodium deficit. Three patients with high intakes, on the other hand, although showing an occasional day of negative balance, retained sodium. The differences in intakes and balances are significant. Three additional patients on high sodium intakes, studied only through the eighth day, remained in positive balance.

Determinations of the serum sodium concentration during the second week were generally in the normal range. The only exceptions were two patients with complications and one patient who developed a late cumulative sodium deficit.

D. Reproduction of the Initial Sodium Balance Trends in Patients with Complications

The development of complications was observed to interrupt the usual trend of sodium changes, reproducing the initial pattern, in two cases. Surgical closure of the wound dehiscence in one of the patients with initial hypernatremia (Case 23) occurred on the fifth day, when sodium loss would customarily have been anticipated. Rather than eliminating sodium, however, the patient retained it. Sodium elimination was delayed until the eighth day after closure of the perforation. The patient's serum sodium concentration fell despite sodium retention on the second postoperative day, rose above normal on the fourth day, and underwent a second "paradoxical" fall following closure of the dehiscence. The patient developing the subdiaphragmatic abscess and pyloric obstruction (Case 18) showed renewed fluctuations before and after his operations, and the swings which took place were of a greater than average magnitude (Chart 6).

E. High Initial Urine Sodium Concentration Indicating Relatively Greater Water Retention

The concentration of sodium in the urine was higher on the day of perforation than on any other day during the study (average: 87 mEq/L.). This concentration indicates a proportionately greater retention of water than sodium. The hourly urine volume averaged only 50 cc. in spite of a 204 cc. intake. In the succeeding days the volume of urine rose, but the high sodium concentration was not maintained. The level dropped to 72 mEq/L. for the first and second postoperative days, rose transiently to 80 on the third day, and then fell slowly to 69 mEq/L. on Day 7. On the ninth postoperative day when oral feeding was reestablished, the concentrations rose again to the 80's and remained there for the rest of the period of study.

F. Sodium Concentration of Gastric and Peritoneal Fluid

The sodium concentration of gastric contents was analyzed in 15 patients and that of peritoneal fluid in 4. The concentration in the gastric contents was low on admission (average: 69 mEq/L.) and tended to fall. The average by the third day was 48 mEq. per liter. The concentration in the peritoneal fluid was more variable, ranging from 90 to 162 mEq., in only one case exceeding the serum sodium level.

G. Gastric, Urinary, and Fecal Sodium Losses

On the day of operation and the first two postoperative days, gastric sodium losses varied from 9 to 87 mEq. a day (0.2 to 2.7

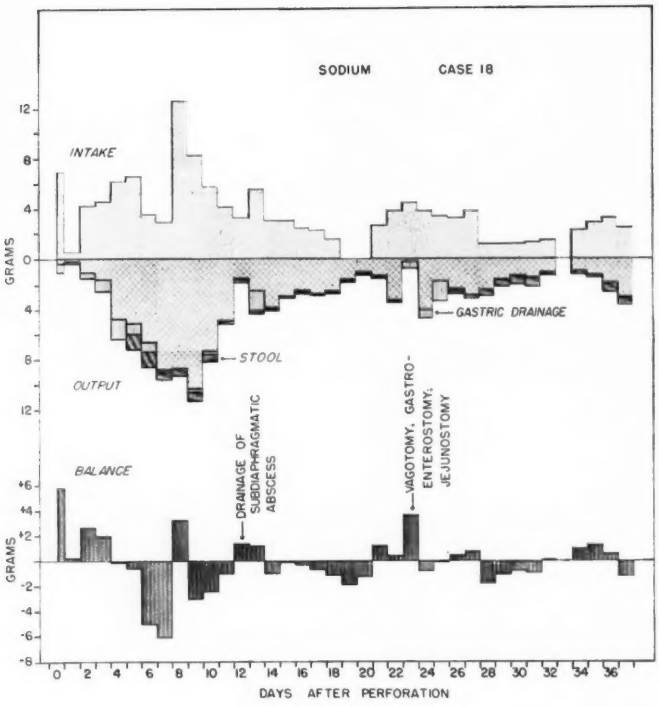


Chart 6 (Case 18).—Reproduction by secondary trauma of the original trend of sodium retention followed by sodium elimination. A subdiaphragmatic abscess developed in this patient and was drained on the 12th day. Later, pyloric obstruction necessitated surgical relief on the 23d day. Sodium retention and subsequent sodium elimination were associated with each of three operations. The order of magnitude of the changes was greatest after the initial trauma.

gm.), diminishing gradually thereafter except in two patients who had outputs on single days of 117 and 104 mEq. (2.7 and 2.4 gm.), (see Table 8, Paper VI).[18] Patients with higher gastric fluid losses had greater sodium outputs. Ten patients with an average daily output of 482 cc. in the first three postoperative days lost 35 mEq. (0.8 gm.) of gastric sodium a day, while seven with an average gastric fluid output of 944 cc. lost 56 mEq. (1.3 gm.) a day.

Urinary sodium losses varied from 9 to 383 mEq. a day (0.2 to 8.8 gm.) during the first postoperative week, but outputs exceeding 150 mEq. (3.5 gm.) were observed only following infusions of 175 mEq. (4.0 gm.) or more of sodium.

Fecal sodium losses were small and stools infrequent; the largest daily loss in any case was 83 mEq. (1.9 gm.), and the average was only 9 mEq. (0.2 gm.).

INTERPRETATION OF SODIUM OBSERVATIONS

A. SIGNIFICANCE IN REGARD TO THE PLAN OF FLUID THERAPY

The sodium observations afford convincing evidence that the cells of these perforated ulcer patients were not deprived of large quantities of water during the formation of peritoneal edema. To provide sufficient osmotic pressure to withdraw fluid from the cells, the total solute concentration of the extracellular fluid must be high. Specifically, the extracellular sodium and chloride concentrations must be high, since they comprise the major portion of the extracellular solutes. Withdrawal of nearly 5 liters of fluid, as suggested by the thiocyanate and sodium volumes,[1] could only have occurred if the extracellular sodium concentrations had risen 10 or 15 mEq/L. above the levels actually observed. The average serum sodium concentration did not exceed 139.4 mEq/L. at any time during the first four days, and no level above 151 mEq/L. was recorded in any

case. Expansion of the extracellular fluid at the expense of cell water can be ruled out on the bases of these data alone, but additional evidence is available which refutes it further. The amount of sodium retained would not have been large enough to maintain the observed serum sodium concentration if 5 liters of water had entered the extracellular space from the cells.#

If the therapy of our patients were evaluated only in the light of the changes in serum sodium concentration, it would be concluded that in the early days after perforation too little sodium had been given, since the concentrations tended to fall. In view of the sodium balances, on the other hand, the patients would appear to have been given too much, since they received more sodium than they excreted. This apparent conflict is dissipated by a simple accounting, pointing to greater retention of water than sodium. During edema formation with displacement of sodium and water into the interstitial spaces, concomitant retention of water and sodium occurred. The ratio of water to sodium, however, was greater than is normal for the extracellular fluid. This explanation is supported by the early positive fluid balance and the high initial urine sodium concentration. The so-called "paradox" is more apparent than real. A paradox would have existed if the serum sodium had failed to fall or the body did not retain sodium. Calculations indicate that no more than 3.5 liters of edema fluid need have formed to explain the location of the "missing" sodium in any of the cases, and in the average case 1.2 liters is sufficient.

If the 3 to 11 liter increases in extracellular fluid volume suggested by the thiocyanate and the Na^{24} expansions had occurred in these patients, they would have required mobilization of substantial amounts of sodium from some storehouse outside the extracellular compartment. Bone is known to be such a storehouse.* Sufficient data are available to permit calculation of this amount in 12 cases. With correction for Gibbs-Donnan equilibrium, the average quantity of sodium that would have to be mobilized in these cases to maintain the serum sodium concentration despite the observed thiocyanate expansion is 534 mEq. This quantity is more than half the entire store of sodium outside the extracellular space.† The improbability that this amount of sodium is mobilized in the short period between perforation and peak thiocyanate expansion lends support to the clinical impression that edema formation after perforation does not exceed 3 to 4 liters.

Having dealt these blows to the concept of extracellular expansion at the expense of cell water, we find that we have escaped from one paradox into another. If there is only sufficient sodium available to maintain the serum sodium concentration in 1 to 3 liters of edema water and none is left over to go into soft tissue cells or bone, how can the expansion of the radioactive sodium space be explained? One possibility is the extravascular binding of the radioactive ions. A second is that after trauma there may be a more rapid turnover of sodium between extracellular fluid and bone. If after perforation the exchange of injected Na^{24} with bone Na^{23} is accelerated, the quantity of radioactivity recovered from the serum 50 minutes after injection will be lower than under normal conditions. Either of these possibilities would lead to calculation of an unduly large extracellular fluid volume. No matter which of these explanations holds, however, the quantity of fluid required by the ulcer patient remains the same. Sufficient fluid must be given to maintain the circulation, to support organ function, and to meet the urinary, gastrointestinal, and insensible

It will be recalled that in the first paper of this series [1] it was shown that careful fluid balances excluded exogenous water as the source of the extracellular fluid expansion.

* References 19 through 21.

† Deane and Smith report figures for total sodium and extracellular sodium in five adult males which average 2700 and 1772 mEq.[22] Moore and associates report a normal range of 2700 to 3000 mEq. for total body sodium in the healthy 70-kg. adult male with extracellular sodium of 1800 to 2000 mEq.; references 13 and 23.

losses. Less than a liter need be planned to combat cellular dehydration, provided therapy is prompt and adequate.

We can only conjecture as to the factors responsible for the excessive dilution of injected thiocyanate ions. Binding of the thiocyanate by protein or other large aggregates extravascularly may play a role.

B. Significance of the Sodium Observations in Regard to the Plan of Electrolyte Therapy

In planning sodium therapy for perforated ulcer patients, it must be recalled that the fall in serum sodium concentration in these patients is on a different basis from the falls in serum potassium and phosphorus. The drop in sodium concentration is due predominantly to a disproportionate retention of water. Most of the sodium remains in the body, and that which is displaced into the peritoneal tissues will return to the circulation when the edema is resorbed. In contrast, external losses are the major cause of the falls in serum potassium and phosphorus levels. Therefore, intracellular electrolyte replacement should be vigorous, but no attempt should be made to maintain the serum sodium concentration.

Moderation in early sodium administration is also suggested by comparison of the sodium elimination of patients receiving a low sodium intake with that of patients receiving a high intake. We have no evidence that the patients receiving a high dosage fared differently from the low-intake group, but the subsequent sodium elimination was delayed a day or two in those on the higher intakes. During the period of edema formation, sodium is needed in therapy. The plasma volume should be maintained and external sodium losses replaced, but excessive sodium administration appears to present later a problem of disposal. The possibility of prolonging edema by overenthusiastic sodium therapy is, therefore, to be kept in mind throughout the first five or six postoperative days.

Sodium elimination, once under way, progressed to a cumulative sodium deficit in at least five cases. This occurred during the second week, when an oral intake of milk and cream had supplanted intravenous feeding. We have no evidence that the deficit was detrimental, but it may be wise to supply a small amount of sodium in this phase.

Chloride Observations

Chloride studies were carried out in 20 patients. The concentration of chloride in the serum was measured with sufficient frequency in 17 to determine the trends. Balance data were obtained in all but 3 of the 17.

In the postoperative period chloride changes were similar to but not identical with those reported for sodium.

A. The Initial Chloride "Paradox"

The serum chloride concentration fell in the majority of the patients during the time chloride was being retained. The retention of chloride differed from that of the sodium in that it was of shorter duration. A typical case is shown in Chart 7.

1. *Early Chloride Retention: Its Exaggeration by Chloride Administration.*—The initial period of chloride retention lasted one to three days, one day being the commonest. All the patients were in positive balance on the day of perforation, but by the first postoperative day 8 of the 14 had started to lose chloride. Despite this early turn toward negativity, cumulative chloride balances, which can be calculated for 12 cases, were still positive at the time of peak thiocyanate expansion in 9. One of the remaining three cases, the patient with the subdiaphragmatic abscess, did not reach peak thiocyanate expansion until the ninth postoperative day (Case 18).

Increasing the chloride intake in this initial period increased chloride excretion as well, but the increase in output was not proportional to the rise in intake, resulting in exaggeration of the chloride retention. On the day of perforation, six cases receiving an average intake of 1.6 gm. retained 1 gm. (28 mEq.). Three cases receiving an average of 6.8 gm., on the other hand, retained 2.6 gm. (73 mEq.), although their outputs rose to 4.2 gm.

2. *The Postoperative Fall in Serum Chloride Concentration.*—Serum chloride concentrations were generally high on admission and showed a subsequent fall. Of 14 patients whose chloride concentrations were measured on entry, 5 showed high normal levels (105 or 106 mEq/L.) and 6 greater than normal levels (107 to 115 mEq/L.). There were three in the subnormal or low normal range (94, 98, and 100 mEq/L.).

The serum chloride concentrations fell in 12 of the 14 patients during the early post-

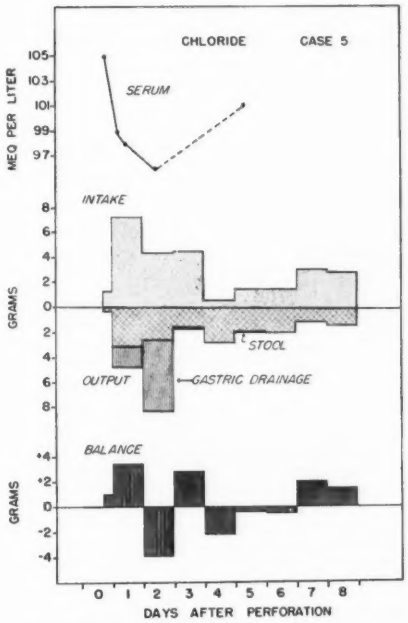


Chart 7 (Case 5).—The serum chloride concentration and chloride balance: Chloride retention on first postoperative day and subsequent variability of balance. The serum chloride level fell during initial positive chloride balance. The balance shows the variability seen in many of the patients. Fluctuations in gastric drainage, as well as in intake, contributed to this variability.

operative phase. Chloride retention in 11 of these coincided with the fall. In five patients followed regularly, concentrations of 100 mEq. or below were reached by the second or third day. Three patients whose levels were only occasionally measured also showed subnormal concentrations at this time. One of the two who displayed a rise was the patient with the lowest initial concentration (94 mEq/L. one hour after perforation, Case 6). The other started with a concentration of 105 and showed a rise to 114 mEq/L.

B. The Subsequent Rise and Fall in Serum Chloride Concentration

Like the serum sodium, the serum chloride concentration rose transiently on the third postoperative day and then exhibited a secondary fall. The chloride rise was of shorter duration and the subsequent period of low concentration longer than was the case with the sodium. Only in two cases was a rising serum chloride concentration observed during chloride elimination, a second apparent paradox.

C. Variability of the Chloride Balance After the Initial Retention

While the serum chloride concentration was rising and falling again, variability characterized the chloride balances. Alternation of days of negativity with days of positivity was common. Differences in the volume and quantity of gastric drainage and wide fluctuations in intake accounted for the lack of uniformity in the balance changes. Two patients on prolonged nasogastric suction developed cumulative deficits of 155 and 245 mEq., while six others on higher intakes or requiring shorter periods of gastric drainage developed positive cumulative balances ranging from 141 to 814 mEq.‡ Three patients shifted irregularly between retention and depletion.

High chloride intakes during these later days after perforation had the same effect as during the immediate postoperative period: increasing the output yet rendering the balance more positive.

D. Late Variability of Balance and Serum Concentration

During the second week after perforation, both the chloride balances and the serum levels varied irregularly. Patients whose

‡ The balance calculations do not include losses in sweat.

postoperative courses were smooth tended to retain chloride if given more than 2 gm. a day and to lose it if given much less. Six patients showed a rebound of the serum chloride concentration to higher than normal levels, while subnormal concentrations persisted in three. Normal concentrations were encountered in the remainder.

No close correlation existed between the late serum chloride concentrations and the cumulative or day-to-day chloride balances. Of the patients showing late hyperchloremia, three had cumulative balances of more than 282 mEq. (10 gm.), two showed only mild retention, and one had an actual chloride deficit.

E. Repetition of the Initial Balance Trends in Patients Developing Complications

In two patients the chloride balance was followed throughout the development of complications. A repetition of the initial balance trends occurred in each. Case 18, after each of his operations, first retained and then eliminated chloride.

F. Chloride Concentration of Stomach Contents and Free Peritoneal Fluid

1. *The Chloride Concentration of Gastric Contents.*—The gastric contents of 15 patients were anlayzed for chloride. The admission concentration varied from 29 to 128 mEq/L. in the patients operated on and was 144 mEq/L. in the case without operation. The average initial concentration was 90.5 mEq/L. In 10 cases serum chloride concentration exceeded gastric chloride concentration, and in 5 the gastric concentration was the higher. On the following day, the average gastric chloride level rose to 98.9 mEq/L. and in six patients the gastric level exceeded the serum concentrations. Thereafter, the gastric concentrations tended to fall below the serum levels, although higher levels were seen intermittently in five cases.

2. *The Chloride Concentration of Peritoneal Fluid.*—The chloride concentration of peritoneal fluid was measured in two patients. The concentrations were 120.1 mEq. and 105.8 mEq., the former exceeding the serum concentration by 5.1 mEq. and the latter exactly equaling the serum level.

Interpretation of Chloride Observations

A. Significance in Regard to the Plan of Fluid Therapy

The chloride data, like those for sodium, refute the concept that any considerable quantity of fluid is withdrawn from the cells to expand the extracellular space. At no time was the chloride concentration high enough to have contributed to a significant rise in osmotic pressure outside the cells, and the observed fall in chloride concentration was not low enough to indicate a dilution of more than 1.2 liters. Furthermore, the concentration of chloride in bone is even lower than that of sodium, and there is, therefore, presumably less chloride available for mobilization.

B. Significance of the Chloride Observations in Regard to the Plan of Electrolyte Therapy

Although the serum chloride concentrations fell in the majority of the patients, the fall was not primarily due to chloride loss. Disproportionate water retention was responsible. Had no fluid other than isotonic saline been given, displacement of fluid and electrolytes into the interstitial tissues of the peritoneum would have left the serum chloride unchanged. However, water was given as well as saline, and the patients retained it in excess of the salt. This excess was subsequently eliminated.

Chloride therapy should not be aimed at combating the serum chloride drop, lest chloride overloading result and make edema resorption more difficult. On the other hand, if chloride is withheld from these patients because of their tendency to retain it, a low salt concentration may develop. Were the low concentration confined to the chloride ion, we are not convinced it would be harmful, since this ion could be replaced by bicarbonate. A compromise is to be made, however, in which stabilization of the serum chloride concentrations is not attempted, but

chloride is given to compensate for skin and gastrointestinal losses. The need for such replacement is obvious in patients on prolonged nasogastric suction.

SUMMARY AND CONCLUSIONS

The sodium and chloride balances were studied in patients with perforated peptic ulcers: the sodium balances in 15 and the chloride balances in 14.

Retention of sodium and chloride is a characteristic feature of the immediate postoperative period in patients with surgically closed perforated ulcers. This retention can be exaggerated by overenthusiastic electrolyte therapy, since on the first day or two sodium and chloride excretion does not keep pace with intake.

The serum sodium falls as sodium is retained. This so-called "paradox" results from a greater retention of water than of sodium, rather than from an accumulation of sodium within the cells. The observation of early chloride retention associated with a falling serum chloride level is similarly explained.

Sodium and chloride therapy during the initial two days should make good the anticipated sodium chloride losses, but not attempt to combat the drops in serum sodium and chloride concentrations.

Resorption of salt-containing edema water after the second day may result in a second apparent paradox: the sodium or chloride concentration rising during salt elimination. This is due to greater loss of water than salt.

Cumulative sodium deficits develop in the latter part of the first postoperative week if the diet is poor in sodium.

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CORRECTION

In the article "Adrenal Cortical Steroids Following Elective Operations," by R. Elman, T. E. Weichselbaum, J. C. Moncrief, and H. W. Margraf, in the November, 1955, issue of the Archives, the sentence beginning on the fifth line from the end of the right-hand column of page 702 should read "In three patients, compound F was infused before and 24 hours after either unilateral or bilateral adrenalectomy for advanced carcinoma of the breast."

The Subclavian Vein, a Constant and Convenient Intravenous Injection Site

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The technical aspects of starting intravenous infusions have been abundantly discussed in the literature. While in the great majority of cases intravenous medication can be started with little difficulty and time loss, a substantial number remains where the patient's condition, the requirements of surgery, or other limiting factors make this procedure time-consuming and sometimes it is impossible to start a completely satisfactory intravenous drip. In the operating room a cut-down can be performed on these patients. This requires additional time, and its application is further restricted by the limited number of suitable veins. Consequently, anesthetic techniques may be modified to eliminate intravenous medication, and occasionally unnecessary risks are taken by administering anesthesia for major surgery without having a vein cannulated.

The difficulties in starting infusions are multiplied in pediatrics to the point where technical considerations may unduly influence the decision to administer parenteral fluids. The same is true in traumatic work where limbs may be injured and burned, obscuring the conventional sites and landmarks for cannulation. It is entirely within the realm of possibility that in the event of a national disaster the use of adequate infusions may constitute a major bottleneck in the care of the victims. Under such conditions cut-downs will be out of the question for lack of time and sterile equipment. Physicians will be called on to start infusions only where the trained auxilliary personnel failed. The efficiency of the profession would be greatly increased if a technique were available by which a vein could be cannulated rapidly and consistently in every patient regardless of age and circulatory status. Such a procedure would in all probability be also welcome in the everyday routine of receiving rooms and surgical wards.

For these reasons the recent description of a technique by which infusions can be started consistently in the subclavian vein [1] attracted our attention. The original claims were confirmed from other institutions * and were subsequently extended by a series of impressive angiograms.[4] Since knowledge of this approach may be of considerable practical importance in certain cases and would assume added significance in a national emergency, it was decided to investigate its possibilities.

This study was undertaken to find out (*a*) the consistency and (*b*) the speed with which the subclavian vein can be cannulated, as well as (*c*) the incidence of failures and injuries to surrounding structures.

MATERIAL

Experiments were performed on corpses in the morgues of Ancker, St. John's, and St. Luke's Hospitals in St. Paul. Most of these corpses came subsequently to autopsy. During the period of investigation approximately 80% of all autopsies were included in this series, and, save for the rejection of a single corpse, there was no selection of subjects. As the investigations progressed, a few clinical cases were also added. In the corpses cannulation

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* References 2 and 3.

was attempted with 14- and 18-gauge needles, measuring 3 and 4 in. in length. In the clinical cases and some of the bodies of stillborn babies smaller needles were employed.

METHODS

The needle attached to a syringe containing a small amount of liquid was inserted below the junction of the inner and middle third of the clavicle. As soon as the skin was pierced, suction was applied and the needle was cautiously advanced in a medial, slightly cranial, and slightly posterior direction, hugging the under surface of the clavicle. The fibrous costoclavicular ligament was felt as a distinct resistance and beyond that a lower resistance was felt as the needle entered the vein. In clinical cases the syringe filled rapidly with blood; in corpses the flow depended upon the extent of clotting in the vein and was often obtained only after slight manipulation of the needle. In most corpses the procedure was repeated on the opposite side.

As soon as the needle was placed, the autopsy was started in the customary manner. After the chest was entered, the dome of the pleura was palpated for any evidence of puncture by the needle and the large veins were dissected to demonstrate the location of the needle tip. The course of the needle was not dissected, but an effort was made to palpate it bimanually and determine its relation to the subclavian artery and the trunks of the brachial plexus. In cases where dissection could not be performed, free flow of blood was taken as evidence of a successful tap.

TABLE 1.—*Preliminary Series (No Cranial Angulation)*

Outcome	Number	
Successful	4	
Questionable	5	
Failure	2	(Lung pierced) (Needle in innominate artery)

TABLE 2.—*Main Series (Cranial Angulation); 139 Attempts on Seventy-Six Subjects; Fifty-Six Dissections*

Gross outcome	Number	Per Cent	
Successful	130	94	
Questionable	3	2	
Failure	6	4	(No injuries)
Age distribution of successful attempts			
Adults	120	93	
Children (1 to 10 yr.)	4	3	
Infants (less than 1 yr.)	6	4	
Number of tries in successful attempts			
1	88	68	
2	29	22	
3+	13	10	
Depth of vein in successful attempts			
1.5 in.	38	29	
2 in.	69	53	
2+ in.	23	18	

RESULTS

In a preliminary series of 11 cases the cranial angulation of the needle was neglected. The results of this series are presented in Table 1. The data of the main series are shown in Table 2.

COMMENT

The results should be interpreted with the understanding that in autopsy material conditions are, of necessity, less favorable for the cannulation of veins than in living subjects. Suboptimal conditions, however, are desirable for this type of study.

During autopsy considerable pressure was exerted on the protruding portion of the needle shaft by the reflected flap of thoracic muscles, breast tissue, and skin. In addition, the transection of the first rib and the clavicle in the immediate proximity of the needle produced more disturbance than could be reasonably expected under clinical conditions. In spite of this the needle never became dislodged, even though the shaft bent on a few occasions under the weight of the skin flap. A possible explanation for this is that, whereas in conventional intravenous taps the fulcrum of the excursions of the needle is the skin, in this position the fulcrum is the tough costoclavicular ligament. This change in the mechanics limits the mobility of the needle tip.

The present experiment does not permit the evaluation of the damage that may have been done by the unsuccessful attempts at finding the vein. It should be noted that a second attempt was necessary in less than one-third of the cases and more than two attempts in only about 10%. Injury to nerves cannot be excluded with certainty, but the vagus and phrenic nerves run in a plane that is medial and posterior to the correctly placed needle tip, whereas the brachial plexus lies posterior and lateral to its course.

Infiltration of an infusion in this position was encountered in a single case. In an unconscious patient after the unobstructed infusion of 200 ml. of fluid, a swelling of the anterior and lateral triangles of the neck was noted. The fluid collected outside the deep cervical fascia and did not interfere with respiration or circulation. This case is mentioned because infiltration in the vicinity of the upper mediastinum is the potentially gravest complication of this procedure.

Contrary to expectations, the pleura was never pierced in this series when the proper technique was used. The explanation is probably that if the needle touches on the pleura at all it does so at a tangent in a region where there are no bony attachments and the pleura yields readily.

CONCLUSIONS

Cannulation of the subclavian vein is not intended to replace conventional methods. It is suggested, however, that in difficult cases two attempts could be made on each side before a cut-down is started.

Under relatively adverse conditions the vein could be entered in better than 90% of the cases and in more than 90% of the successful attempts one or two attempts only were necessary, corresponding approximately to a time expenditure of 60 seconds or less. The needle proved to be remarkably safe against dislodgment.

With proper technique there was no evidence in the series of injury to any of the vital structures in the vicinity. Carelessness, however, may produce grave injuries, as shown by the results of our preliminary series.

The vein is large enough to accommodate every commonly used gauge needle. Short bevels are preferable and there is nothing gained by using too small a needle. Seldom if ever is a needle longer than 3 in. required, and a 2-in. needle will suffice in more than 80% of the cases. In children and small persons the distance between the proposed site of skin puncture and the midline gives a useful estimate of the required needle length.

The subclavicular area is accessible to the anesthesiologist during most surgical procedures, eliminating the necessity of arm boards. Infusions can be started on the same side on which the blood pressure cuff is applied, leaving the opposite side free for surgery. Adequate-size needles may be inserted even in infants, making prompt blood replacement during surgery easier. The needle can be secured with a few strips of tape, and fewer restraints are needed with uncooperative subjects than previously.

Inserting a large needle into the chest of a subject appears frightening at first sight. It should not be undertaken without accurate knowledge of the topographical anatomy of the retroclavicular region. The modest time and effort spent on the subject, however, may prove lifesaving in emergency situations and will save the day in many others.

SUMMARY

The possibility of cannulating the subclavian vein was investigated in autopsy material. It was successful in more than 90% of the cases, and it could be achieved within 60 seconds in over 90% of the successful tries.

In no case did the properly inserted needle injure the important adjacent structures, but accurate knowledge of the topography of the region is essential for the safe performance of this procedure.

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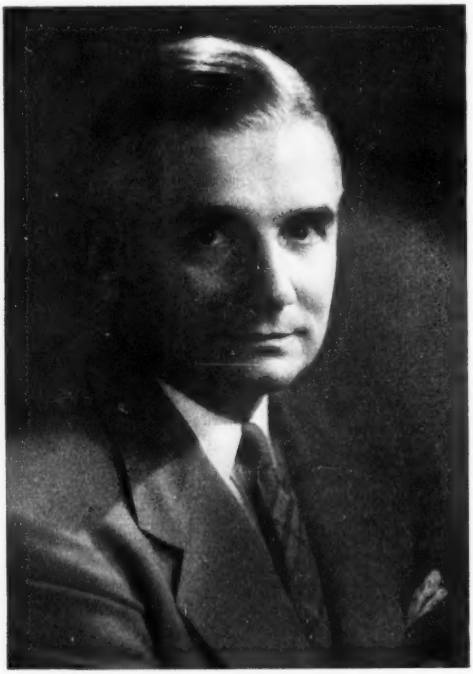
Obituaries

HOWARD K. GRAY, M.D.
1901-1955

Howard Kramer Gray, 54 years of age, accidentally drowned in Lake Pepin, late in the afternoon of Sept. 6, 1955, while swimming in an attempt to recover a dinghy that had been swept away from his cabin cruiser by a strong wind. Lake Pepin is a widening of the Mississippi River where it courses between Minnesota and Wisconsin.



DR. HOWARD K. GRAY
1901-1955

Born of nationally known parents, Howard Gray, familiarly known as "Howdie," entered Princeton, in 1919, from the Gilman School. In 1922, his senior year at Princeton, he played left end on a famous football team that defeated a strong University of Chicago team, by which Princeton had been beaten the year before. In the fourth quarter of the game, with the score 18 to 7 in favor of Chicago, Howdie caught a pass intended for a Chicago player and ran for a touchdown. He went over again from the 2 yard line and the game ended with the score 21 to 18 in Princeton's favor. This game, according to

Read at the meeting of the Society of Clinical Surgery, New Orleans, Nov. 11 and 12, 1955.

many sports writers and football coaches, was one of the football classics of all time. The high esteem in which Howdie was held by his classmates, and by the officers of the university, was evidenced by his being chosen to represent the class when disciplinary action against it was contemplated by university authorities.

After his graduation from Princeton, Howdie spent two years at the University of Nebraska College of Medicine, Omaha. He then transferred to Harvard Medical School, from which he received the degree of doctor of medicine in 1927. After an internship that he served at the Robert Packer Hospital, Sayre, Penn., he entered the Mayo Foundation, Graduate School, University of Minnesota, in 1928. He received the degree of master of science in surgery from the University of Minnesota in 1932. He was surgical first assistant to Dr. Donald C. Balfour and to Dr. E. Starr Judd. From them he acquired not only intense interest in the surgical treatment of diseases of the upper part of the abdomen, but he learned from his chiefs and their medical colleagues the best treatment to use in the most complicated conditions.

With his skill in surgical diagnosis and treatment, Dr. Gray combined sympathetic understanding of the personal problems of patients, all of whom regarded him as their friend. Sir Heneage Ogilvie, in *The Lancet* for Sept. 17, 1955, wrote that Dr. Gray was "greatly admired and loved in Britain. . . . In two things he was pre-eminent in a country where good surgery is common. The first was his clinical or bedside wisdom, founded on a long memory of cases each of which had been to him a personal problem. . . . His second outstanding character was his ability as a teacher, as a writer and above all as a speaker."

Early in his surgical career, Dr. Gray developed an interest in thoracic surgery and in his weekly surgical program usually some thoracic cases were listed. He was certified both by the American Board of Surgery, Inc. and the American Board of Thoracic Surgery, Inc.

Dr. Gray's contributions to medical literature, which numbered in the neighborhood of two hundred, dealt mainly with clinical surgery. However, Dr. Gray made several investigations in pathology and published the results. In addition, he was author or co-author of several chapters in leading surgical books. He was co-author, moreover, of a book on malignant lesions of the stomach; a scientific exhibit based on material in this book won the Billings Gold Medal at the Scientific Exhibit of the American Medical Association in 1939.

Before World War II, Dr. Gray joined one of the two Medical Specialists Units of the United States Naval Reserve, organized at the Mayo Clinic. This unit was called to duty on the day of the attack on Pearl Harbor. Dr. Gray served with great distinction as chief of surgery in several naval hospitals, as well as aboard the hospital ship "Solace." He operated almost continuously for a period of thirty-six hours in the course of the attack on Saipan. He reached the grade of captain and was awarded the Legion of Merit. While the war was in progress, he was elected to membership on the American Board of Surgery, Inc.

After the war, Dr. Gray returned to the Mayo Clinic, and, shortly afterward, he became a member of its Board of Governors.

In 1949 he received the honorary degree of doctor of science from Lafayette College, and, in 1954, he received the same degree from the University of Nebraska. In 1951 he presented the Moynihan Lecture at the Royal College of Surgeons, in London, and was made an honorary member of the Surgical Section of the

Royal Society of Medicine. In addition to his being a fellow of the American College of Surgeons and a member of the American Medical Association, he was a member of the Society of Clinical Surgery, the American Surgical Association, the Southern Surgical Association, the Western Surgical Association, and the American Association for Thoracic Surgery. At the meeting of the American Surgical Association in May, 1955, he presented the results of a study on "Obstruction of the Duodenum Beyond the Ampulla of Vater: A Possible Cause of Symptoms Suggesting Disease of the Biliary Tract."

To give a short description of Howard Gray as a man is difficult; yet some comments that appeared in a publication of the Mayo Clinic, for reading by members of its staff, appealed to me: ". . . there was a storybook quality about Howdie Gray, the sort of story that a medical man would like his teen-aged son to read and emulate. He was a brilliant student, yet the captain of his college football team, a superior Fellow of the Mayo Foundation and a great team man as Clinic Consultant; an incomparable medical teacher, lecturer and writer; an outstanding surgeon and Clinic executive; a decorated navy officer. . . . He liked everyone, and so far as I know every man or woman he ever met returned the feeling."

And from the *News Bulletin,* a publication of St. Marys Hospital, in Rochester, for September, 1955, comes the following:

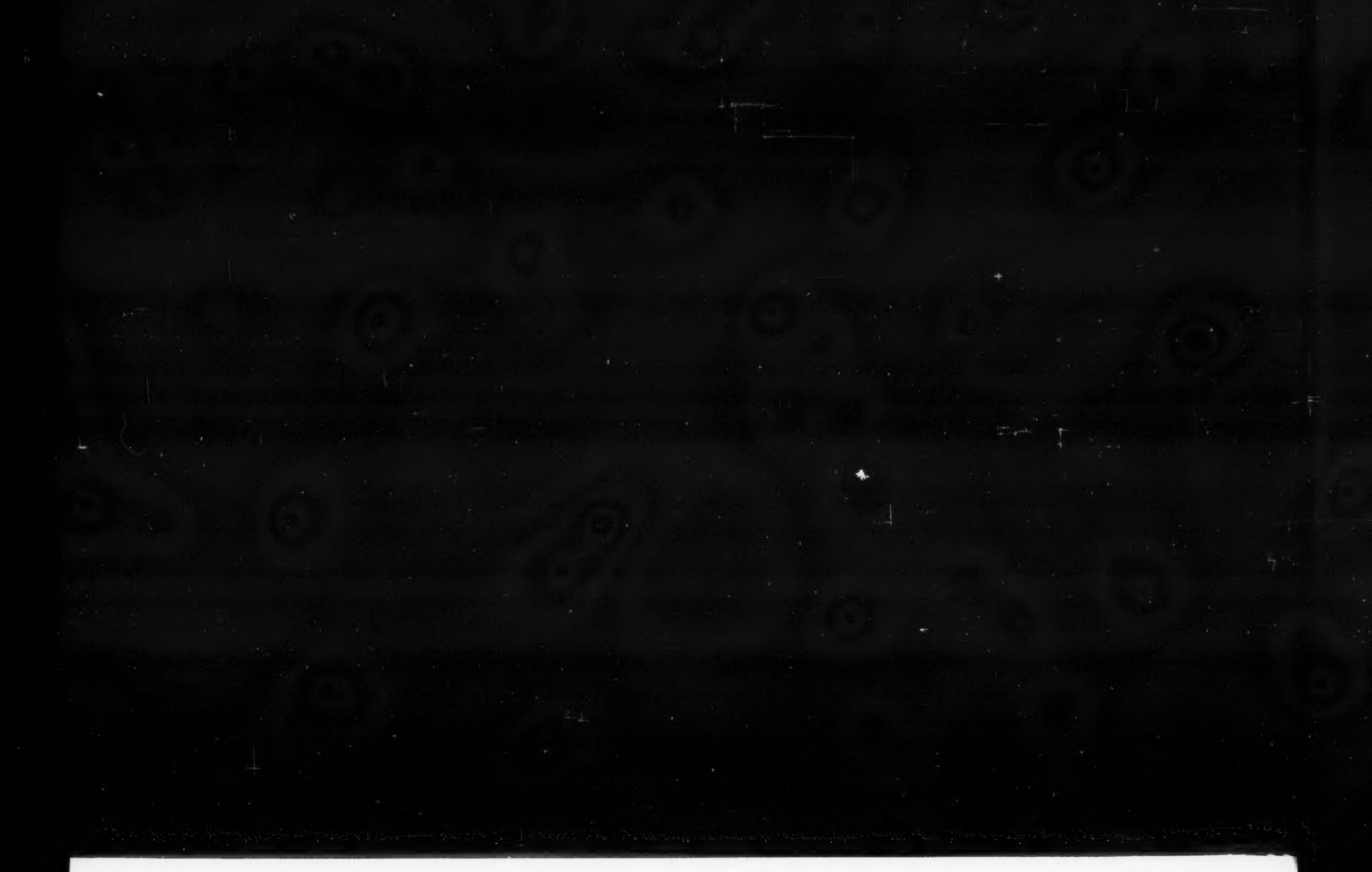
HOWARD K. GRAY, M.D.

To his family—
a loving husband and father.

To his patients—
a skilled surgeon, personally interested in their welfare.

To his surgical team—
an exemplary teacher and friend.

To all—
the sisters, the nurses, the personnel at St. Marys—a fine Christian gentleman, whose informal "Hi!" meant joy, peace, and genuine charity.

May his soul rest in peace.

WALTMAN WALTERS, M.D.